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СОЧЕТАНИЕ ИНФЕКЦИОННОГО ЭНДОКАРДИТА И ИНФЕКЦИИ COVID-19 У МОЛОДОЙ ПАЦИЕНТКИ

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Combination of Infective Endocarditis and Covid-19 Infection in a Young Patient

Резюме

Инфекционный эндокардит нативного митрального клапана с множественными кардиоэмболическими инфарктами головного мозга и миокарда при сочетании с новой коронавирусной инфекцией тяжелого течения стал причиной неблагоприятного исхода у молодой женщины. Причинами этого стали как поздняя диагностика ИЭ (несвоевременное выполнение трансторакальной эхокардиографии), так и синергия патогенетических механизмов двух тяжелых заболеваний, наиболее ярко проявившаяся в развитии гемореологических нарушений, повреждении миокарда, легких и головного мозга.

Ключевые слова: *инфекционный эндокардит, новая коронавирусная инфекция, SARS COV 2, COVID19*

Конфликт интересов

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

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Abstract

Infective endocarditis of the native mitral valve with multiple cardioembolic cerebral infarctions and myocardial infarctions against the background of a severe new coronavirus infection caused an unfavorable outcome in a young woman. The reasons for this were both the late diagnosis of IE (untimely performance of transthoracic echocardiography) and the synergy of the pathogenetic mechanisms of two serious diseases, which was most clearly manifested in the development of hemorheological disorders, damage to the myocardium, lungs and brain.

Key words: *infective endocarditis, new coronavirus infection, SARS COV 2, COVID19*

Conflict of interests

The authors declare that this study, its theme, subject and content do not affect competing interests

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BP — blood pressure, HIV — human immunodeficiency virus, WHO — World Health Organization, DU — duplex ultrasound, MI — myocardial infarction, ACEI — angiotensin converting enzyme inhibitors, IL-6 — interleukin-6, CT — computed tomography, MK — mitral valve, MRI — magnetic resonance imaging, NIV — non-invasive ventilation, CF — circulatory failure, PCR — polymerase chain reaction, RNA — ribonucleic acid, PASP — pulmonary artery systolic pressure, CRP — C-reactive protein, RR — respiration rate, HR — heart rate, ECG — electrocardiogram, EchoCG — echocardiography, LVEF — left ventricle ejection fraction, FC — functional class, SpO_2 — oxygen saturation, SARS-CoV-2 — Severe acute respiratory syndrome-related coronavirus 2, COVID-19 — Coronavirus Disease 2019, IE — infective endocarditis

The novel coronavirus pandemic declared by WHO on March 11, 2020 [1] made us focus on the state of the cardiovascular system in SARS-CoV-2 patients [2]. The most frequently discussed and obviously most significant cardiovascular disorders are acute coronary syndrome, diffuse myocarditis and acute myocardial damage [2, 3]. These conditions are caused by coagulation dysfunction, endothelial damage, exposure of the myocardium to the virus, pro-inflammatory cytokine release, hypoxia, stress, and other factors [3]. There is no information and evidence of specific COVID-19-mediated endocardial damage. There are few data on other types of endocardial damage, in particular, the incidence of infective endocarditis (IE) during the SARS-COV-2 pandemic [4]. Cases of IE during this period are presented in the publications mainly as clinical observations [5]. Studies devoted to this issue present data indicating, on the one hand, a decrease in the number of reported cases of IE at the peak of the pandemic compared to the same previous period, and on the other hand, a significant increase in in-hospital mortality [6]. IE has an unfavorable prognosis and high mortality [7] even in the absence of concomitant diseases. The similarity of clinical symptoms of severe viral (COVID-19) and bacterial (IE) infections, systemic inflammatory response syndrome, late access to medical care due to severe restrictions on the movement of patients and shifting the focus of the healthcare system to the treatment of coronavirus disease are additional factors contributing to the diagnosis of IE and worsening of its prognosis and outcomes [8].

In the presented clinical case, left-sided IE with embolic syndrome and concomitant severe COVID-19 in a young woman led to an unfavorable outcome.

A 34-year-old woman was admitted to the Infections Department with complaints of general weakness, mixed dyspnea at moderate exercise and rest, and fever up to 38 °C. She had no previous health problems. Two months before hospitalization, two weeks after cesarean section, febrile fever appeared. Ceftriaxone injections, 4 g/day, were prescribed and an improvement in overall well-being and relief of fever were noted. A week later, the patient noted febrile fever with chills again, as well as dyspnea during normal physical exertion; cefepime 4 g/day was prescribed and body temperature returned to normal. Nasal and throat swabs for COVID-19 were negative. Deterioration of the condition on the day of admission: weakness increased sharply, dyspnea at rest appeared. Chest computed tomography (CT) was performed, bilateral pneumonia, 25–35% lung involvement, bilateral pleural effusion were detected, pulmonary infarction could not be excluded.

The patient's state at admission was severe. Oxygen saturation (SpO_2) 94%. Orthopneic position. Lethargy. Pale gray skin. Dense edema and cyanosis of the right lower limb. Muffled, rhythmic heart sounds. At the apex of the heart, I tone is weakened, systolic murmur radiates to the axillary region. II tone accent over a. pulmonalis. Heart rate (HR) and pulse rate is 100 bpm. BP 110/60 mm Hg. In the lungs, breathing is harsh, weakened in the lower parts, no rales. Abdomen is soft, nontender. Diuresis rate is reduced. Complete blood count: RBC 3.63×10^{12}/l, HGB 75 g/l, PLT 113×10^9/l, WBC 7.7×10^9/l, ESR 31 mm/h. Blood creatinine 225 mmol/l. Troponins are positive. D-dimer is positive. C-reactive protein (CRP) 175 mg/l. Ferritin 590 μg/l. PCR for COVID-19 at admission is negative. Procalcitonin 0.85 ng/ml. Blood cultures for sterility are negative. HIV antibodies and viral hepatitis markers are negative.

Electrocardiography (ECG) findings: focal changes in the myocardium of the left ventricle lower wall. When performing echocardiography (EchoCG), akinesia of all segments of the lower wall of the left ventricle was detected, ejection fraction (EF) of the left ventricle (LV) was 36%, pulmonary artery systolic pressure (PASP) was 31 mm Hg. In the projection of the anterior cusp of the mitral valve (MV), a hyperechoic formation 1.4 × 1.1 cm in diameter is visualized. According to the duplex

ultrasound (DU) of the veins of the lower extremities: iliofemoral deep vein thrombosis on the right. Magnetic resonance imaging (MRI) findings: multiple lacunar cerebral infarcts. A gynecologist did not detect any abnormality.

The diagnosis was: Infective endocarditis of the native mitral valve with grade 3 mitral regurgitation. 1st degree pulmonary hypertension.

Coronavirus infection, virus not identified, severe course.

Complications: CF II B (IV FC) according to the Russian classification. Acute kidney injury. Acute respiratory failure. Bilateral pneumonia. Bilateral pleural effusion. Pulmonary embolism. Multiple lacunar cerebral infarcts. Myocardial infarction. Ileofemoral DVT on the right.

In the hospital, antibiotics (imipinem + cilastatin 3 g/day), anticoagulants (fraxiparin 0.3 ml twice times a day) were prescribed, as well as angiotensin-converting enzyme inhibitors (ACEI), beta-blockers, diuretics, gastroprotective agents, mucolytics, oxygen therapy and prone position. Due to bacterial septicemia, steroids and IL-6 inhibitors were not used.

Temperature returned to normal on the third day, weakness and shortness of breath persisted. On day 10, tachycardia (HR 120), hypotension (BP 85/60 mm Hg), and respiratory failure (RR 26 per minute, SpO_2 88%) progressed. As a result, the patient was transferred to the intensive care unit. Due to unstable hemodynamics, dopamine infusion at a dose of 12 μg/kg/min (BP on infusion was 100/60 mm Hg, heart rate — 135 per minute) was prescribed, and non-invasive ventilation (NIV) was initiated. SpO_2 increased up to 90%. The patient was examined by a cardiac surgeon, conservative management was recommended, decision on surgery was delayed until the patient's stabilization. Repeated chest CT revealed bilateral interstitial pneumonia, CT score 3/4 (55–75%), bilateral pleural effusion (Fig. 1).

Repeated throat and nasal swab for COVID-19 was positive. Respiratory and heart failure increased; cardiac arrest in the form of asystole occurred, CPR was without effect. The patient died on the 20th day of hospitalization (10th day in the intensive care unit).

During pathological examination, the myocardium weighs 340 g. The endocardium is smooth, shiny and translucent. On the mitral valve, the overlays are of light yellow color measuring 0.8 × 0.5 cm in size (Fig. 2).

The myocardium is pale red in color, a bluish area measuring 2 × 3 cm is determined on the posterolateral wall of the left ventricle (Fig. 3).

Coronary arteries are not macroscopically altered. The airness of the lungs is reduced, the density is doughy; and the incision of the right lower lobe and left upper and lower lobes showed induration of the tissue of dark red color — lung infarctions (Fig. 4).

In the brain, multiple lacunar small foci are defined, measuring from 1 to 1.5 cm in size, flabby, light yellow in color (Fig. 5).

Histological examination on the mitral valve revealed fibrin masses with the presence of leukocytes (Fig. 2), accumulation of microorganisms; in the myocardium, vacuole and granular dystrophy of cardiomyocytes, foci of necrosis, areas of young and mature granulation tissue along the periphery of necrosis are defined (Fig. 3).

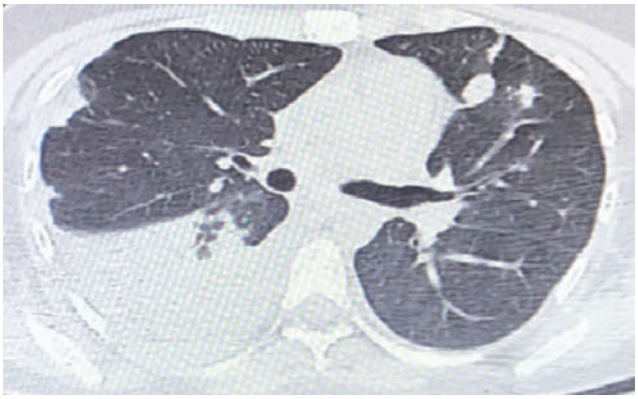

Figure 1. *Computed tomography of a patient's lungs (description in text)*

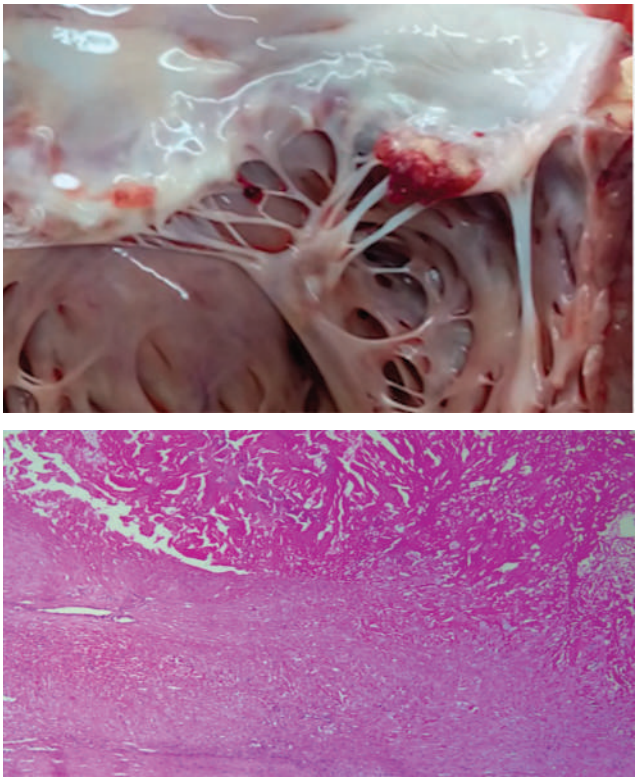

Figure 2. *Vegetations on the mitral valve (photo) and histological signs of fibrin application (hematoxylin/eosin staining)*

In the lungs intra-alveolar edema, multiple pulmonary infarctions of varying onset time were detected; in the lumens of the alveoli, there were accumulations of a large number of hyperplastic desquamated alveolocytes, fibrin masses, lymphocytes and leukocytes (Fig. 4). Multiple small foci of necrosis were found in the brain. SARS-CoV-2 RNA was detected in all the specimens, except for the spleen: in lungs, bronchi, trachea, and myocardium. Unfortunately, the cardiac valve specimen was not examined for the presence of RNA. The pathological diagnosis was the following:

The primary disease: 1. Infective endocarditis of the native mitral valve with grade 3 mitral regurgitation. 1st degree of pulmonary hypertension.

2. Novel coronavirus infection, the virus is identified, acute exudative phase of diffuse alveolar damage.

Primary disease complications: Multiple cerebral infarctions in the left hemisphere. Multiple pulmonary infarctions of varying time of onset. Acute myocardial infarctions (varying periods of onset). Pulmonary edema. Acute kidney injury in the diuretic phase: acute tubular necrosis. Bilateral viral pneumonia.

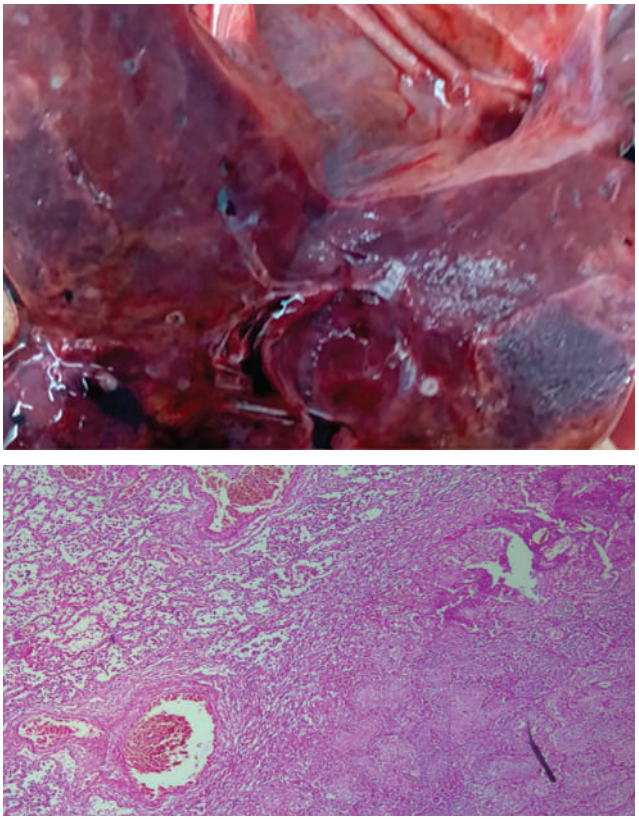

Figure 4. *Lung infarcts (macromedicine and histologicalmedicine)*

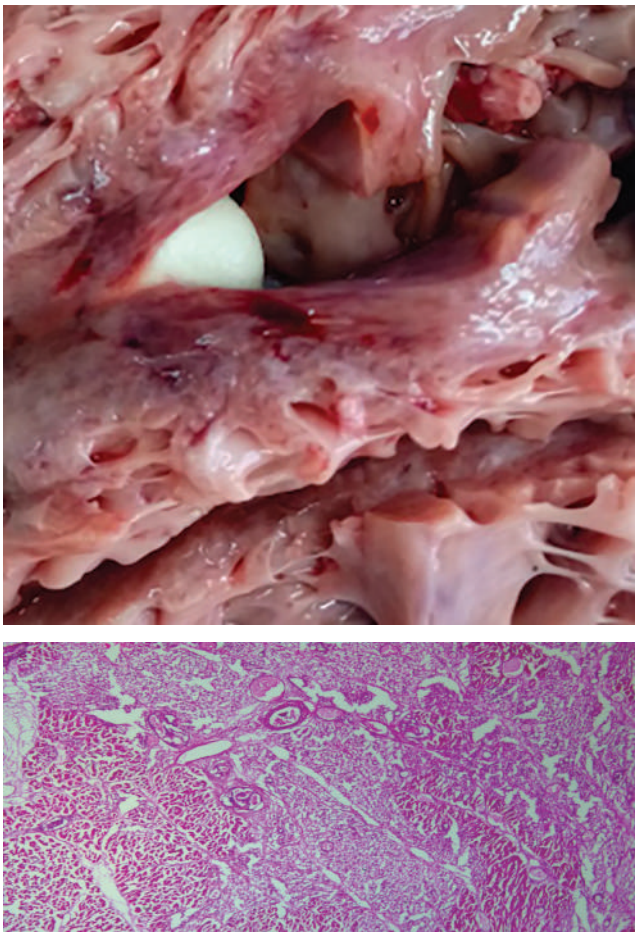

Figure 3. *Left ventricular myocardial infarction (macromedicine and histologicalmedicine)*

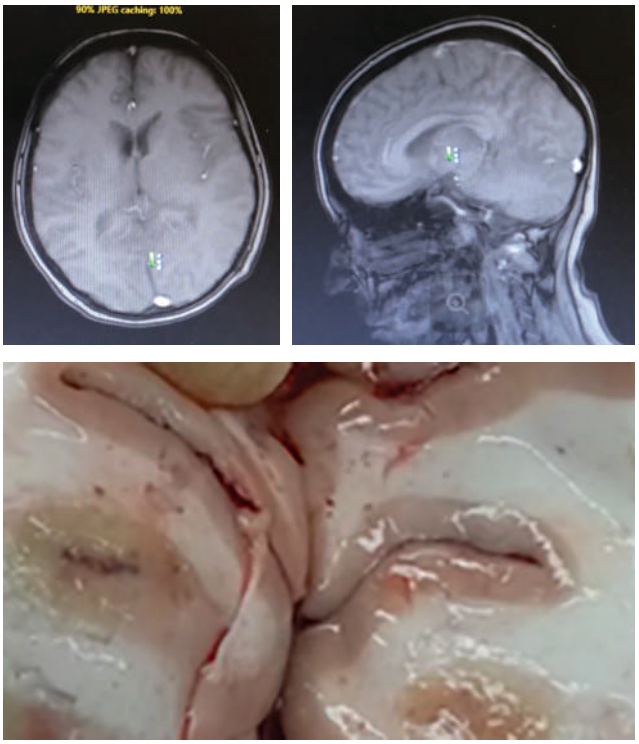

Figure 5. *Cardioembolic lacunar brain infarcts (on MRT and autopsy)*

Discussion

Several aspects of the possible interaction of SARS-COV-2 and IE in this clinical case should be discussed.

Chronology of Severe Viral and Bacterial Infections

An analysis of the sequence of events (febrile wave-like fever with chills, negative PCR results at the time of confirmation of mitral valve IE) suggests the high probability that IE preceded SARS-COV-2 infection. This is indirectly evidenced by the large size of vegetations on the mitral valve and the macroscopic changes in the valve, which take time to form. The late diagnosis of IE, not uncommon at other times [7], during the SARS-COV-2 pandemic is due to the most frequent explanation of any fever by the assumption of this particular infection [6]. This circumstance meant echocardiography was not performed on time, though it was undoubtedly indicated and probably would have been performed at a different time. The simultaneous occurrence of two diseases is not excluded. There is no doubt that they are approximately equal in degree to thanatogenesis (progressive lung damage, multiple thrombosis and myocardial damage characteristic of SARS-COV-2 infection, and cardioembolic cerebral infarctions in left-sided IE).

The Possibility of Endocardial Damage and IE Due to Exposure to Coronavirus

The literature has previously discussed the viral etiology of IE. Fournier P.E. described a case of recurrent IE of presumably enteroviral genesis in a four-month-old baby [9]. However, the viral etiology of IE is justifiably questioned: the direct cytopathic effect of the virus on the endocardium and its incorporation into cells has not been proven. This is particularly why IE is considered an almost exclusively bacterial infection [7], which, in this case, is confirmed by microorganisms in the surface layer of vegetation. Unfortunately, in this specific case, we did not have methods of morphological verification of possible viral damage to the myocardium and endocardium (electron microscopy, immunohistochemistry). Apparently, in this case, the cause of negative blood culture in IE, as discussed in the literature [7, 10], was the previous use of antibiotics.

The State of the Coagulation System and the Use of Anticoagulants

Multiple venous thromboses, damage to the microvascular bed, and signs of systemic hypercoagulation, observed in this particular case, are characteristic of novel coronavirus infection, often cause death and require continuous treatment with anticoagulants [11]. Hypercoagulation and vasculitis are also characteristic of IE. However, the use of anticoagulants is not recommended for the treatment of IE patients or should be used with caution for strict indications, primarily due to the high risk of hemorrhagic stroke. This led to certain challenges in deciding on the use of this group of drugs. Hypercoagulation and large vegetations on the mitral valve contributed to the development of thromboembolic complications of the brain, lungs, and heart.

Synergy of Visceral Lesions and Interpretation of Their Origin in SARS-COV-2 Concomitant with IE

First of all, severe myocardial damage (significant decrease in global contractility and widespread impairment of local myocardial contractility, focal ECG changes) is noteworthy. The possibility of such a lesion exists both with novel coronavirus infection and with IE, and an unambiguous interpretation of the predominant role of either disease in a particular case is difficult even after morphological examination. Damage to the endothelium and thrombosis of large and small branches of the coronary arteries are considered a key mechanism of myocardial damage in SARS-COV-2 infection [11]. In case of novel coronavirus infection, the term "acute myocardial damage" (AMD) is used to refer to conditions accompanied by symptoms of heart failure, rhythm and conduction disturbances, hypotension, and tachycardia with significant increase in serum troponins [12]. Morphologically, this can correspond to diffuse myocarditis, Takotsubo cardiomyopathy, and coronarogenic myocardial necrosis [3, 4, 11]. AMD in COVID-19 occurs with a frequency of 7 to 45%. It often requires hospitalization in the ICU and is always a predictor of an unfavorable outcome [3, 12]. ECG and EchoCG changes characteristic of myocardial infarction (MI), as well as an increase in myocardial damage markers can also be interpreted as a manifestation of coronary embolism in IE with the development of type 2 myocardial infarction [12]. However, in this specific case, macroscopic changes in coronary arteries, as well as microbial emboli in their lumen were not detected. The role of SARS-COV-2 in myocardial damage was likely predominant (decrease in ejection fraction, detection of RNA in the myocardium), which was one of the reasons to avoid surgical treatment of IE.

Conclusion

Infective endocarditis of the native mitral valve with multiple cardioembolic cerebral and myocardial infarctions and concomitant severe novel coronavirus infection caused an unfavorable outcome in the young woman. This was caused by both the late diagnosis of IE (untimely transthoracic echocardiography) and the combination of damaging pathogenetic mechanisms of two serious diseases that mostly affected hemorheology and damaged the myocardium, lungs and brain.

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Пономарева Е.Ю. (ORCID http://orcid.org/0000-0001-6187-7525): интерпретация и анализ данных, подбор литературы, редактирование статьи

Кошелева Н.А. (ORCID http://orcid.org/0000-0001-5585-946X): ведение пациентки в клинике, идея и описание клинического случая, подбор и представление рисунков, интерпретация и анализ данных, редактирование статьи

Author Contribution:

All the authors contributed significantly to the study and the article, read and approved the final version of the article before publication

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Список литературы/ References:

1. Fried JA, Ramasubbu K, Bhatt R, Topkara VK, Clerkin KJ, Horn E et al. The Variety of Cardiovascular Presentations of COVID-19. Circulation. 2020;141 (23):1930-1936. DOI.org/10.1161/CIRCULATIONAHA.120.047164.
2. Шляхто Е.В., Конради А.О., Арутюнов Г.П. Руководство по диагностике и лечению болезней системы кровообращения в контексте пандемии COVID-19. Российский кардиологический журнал. 2020; 25(3): 3801. DOI.org/10.15829/1560-4071-2020-3-3801
   Shlyakho E.V., Konradi A.O., Arutyunov G.P. Guidelines for the diagnosis and treatment of circulatory diseases in the context of the COVID-19 pandemic. Russian Journal of Cardiology. 2020; 25(3): 3801. DOI.org/10.15829/1560-4071-2020-3-3801 [In Russian]
3. Сережина Е.К., Обрезан А.Г. Патофизиологические механизмы и нозологические формы сердечно-сосудистой патологии при COVID-19. Кардиология. 2020; 60(8): 23–26. DOI.org/10.18087/cardio.2020.8.n1215
   Serezhina E.K., Obrezan A.G. Cardiovascular Pathology in Patients with COVID-19. Kardiologiia. 2020; 60(8): 23–26. DOI.org/10.18087/cardio.2020.8.n1215 [In Russian]
4. Маев И.В., Шпектор А.В., Васильева Е.Ю. Новая коронавирусная инфекция COVID-19: экстрапульмональные проявления. Терапевтический архив. 2020; 92(8): 4-11. DOI: 10.26442/00403660.2020.08.000767
   Maev I.V., Shpektor A.V., Vasilyeva E.Yu., Novel coronavirus infection COVID-19: extrapulmonary manifestations. Therapeutic Archive. 2020; 92 (8): 4-11. DOI: 10.26442/00403660.2020.08.000767 [In Russian]
5. Dias CN, Brasil Gadelha Farias LA, Moreira Barreto Cavalcante FJ. Septic Embolism in a Patient with Infective Endocarditis and COVID-19. Am J Trop Med Hyg. 2020 Dec; 103(6): 2160-2161. DOI: 10.4269/ajtmh.20-1133.
6. Cosyns B, Motoc A, Arregle F, Habib G. A Plea Not to Forget Infective Endocarditis in COVID-19 Era. J Am Coll Cardiol Cardiovasc Imaging. 2020 Nov; 13(11): 2470–2471. DOI: 10.1016/j.jcmg.2020.07.027.
7. Habib G, Lancellotti P, Manuel J. et al. 2015 ESC Guidelines for the management of infective endocarditis. The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). European Heart Journal 2015; 36: 3075–3123. DOI:10.1093/eurheartj/ehv319.
8. Hussain A, Roberts N, Oo A. 2020. Prosthetic aortic valve endocarditis complicated by COVID-19 and hemorrhage. J Card Surg. 2020; 35: 1348–1350. DOI: 10.1111/jocs.14643.
9. Fournier PE, Charrel R, Raoult D. Viral endocarditis or simple viral disseminated infection? Clin Infect Dis. 2011; 53: 1298. DOI: 10.1093/cid/cir681.
10. Menu E, Gouriet F, Casalta JP, Tissot-Dupont H, Vecten M, Saby L et al. Evaluation of empirical treatment for blood culture-negative endocarditis. J Antimicrob Chemother, 2017;72 (1):290-298, DOI: 10.1093/jac/dkw362.
11. Коган Е.А., Березовский Ю.С., Благова О.В., Куклева А.Д., Богачева Г.А., Курилина Э.В. Миокардит у пациентов с COVID-19, подтвержденный результатами иммуногистохимического исследования. Кардиология. 2020; 60(7): 4–10. DOI.org/10.18087/cardio.2020.7.n1209
    Kogan EA, Berezovskiy YuS, Blagova OV, Kukleva AD, Bogacheva GA, Kurilina EV. Miocarditis in Patients with COVID-19 Confirmed by Imm unohistochemical. Kardiologiia. 2020; 60(7): 4-10. DOI.org/10.18087/cardio.2020.7.n1209 [In Russian]
12. Thygesen K, Alpert JS, Jaffe AS. et al. Fourth universal definition of myocardial infarction (2018). European Heart Journal. 2019; 40(3): 237–69. DOI: 10.1093/eurheartj/ehy462.