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Clinical case of the coronavirus infection in anamnesis with complication

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Abstract: *coronavirus infection, the causative agent of which is SARS-CoV-2, can cause a wide range of clinical manifestations. This infection is especially dangerous for patients with a predisposition to cardiovascular diseases, such as hypertension. Changes in vascular tone under conditions of increased blood pressure, as well as dysfunction of vascular walls under the influence of a viral infection, lead to irritation of the suprasegmental part of the autonomic nervous system, namely the posterior part of the hypothalamus, which provokes the development of sympathoadrenal attacks with panic attacks. This study aimed to demonstrate that comorbid disease of the cardiovascular system occurred after coronavirus infection worsens the course of the initial manifestations of cerebrovascular insufficiency. Patient T., who suffered from COVID-19 in October 2020, was examined in the neurological department of the State Institution «Head medical center of the Ministry of Internal Affairs of Ukraine» in December-January 2020-2021. During the examination of the patient's neurological status, positive pathological reflexes were found: proboscis and Marinescu-Radovichi reflex, foot pathological Strumpell extensor reflex on both sides, and lability of the autonomic nervous system in the form of acrohyperthermia, tremors of the eyelids and fingers of outstretched hands, slight unsteadiness in the Romberg pose. The patient underwent a general blood count, biochemical blood test, Doppler ultrasound of the main arteries of the head, ultrasound of the heart, and electrocardiography (ECG). Special attention should be paid to the results of the Doppler ultrasound of the main arteries of the head: the intima-media complex thickness of the left common carotid artery in the middle third is up to 0.91 mm, in the bifurcation it has a local thickening up to 1.27 mm, the right common carotid artery in the middle third is up to 0.85 mm (normal up to 1.0 mm), in the bifurcation up to 1.04 mm (normal up to 1.1 mm), with partially lost differentiation into layers, echogenicity is not changed. In consequence of the patient's treatment with statin drugs, scavenger-receptors of monocytes are blocked, the number of which on the surface of cells is stimulated by viruses in the presence of infection, and right to them LDL are attached. Blocking of the capture of LDL by phagocytes limits the formation of foam cells, which are the basis of atherosclerotic plaques, and leads to a decrease in the intima-media complex thickness. According to the results of the ultrasound of the main arteries of the head, after six months of treatment, the thickness of the intima-media complex of the left common carotid artery decreased from 0.91 mm to 0.76 mm, the right one - from 0.85 to 0.65 mm.*

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Conclusions. Comorbid diseases occurring under the influence of coronavirus infection, namely arterial hypertension, worsen the course of such slowly progressive disorders of cerebral blood circulation, as the initial manifestations of cerebral blood circulation insufficiency with the development of sympathoadrenal paroxysms with panic attacks. Treatment with statins, anticoagulants, antihypertensive, nootropic, and sedative drugs helps to stabilize arterial hypertension and reduce the number of sympathoadrenal attacks with panic attacks in patients.

Keywords: Covid-19, hypertension, sympathoadrenal system, panic disorder, carotid intima-media thickness.

Introduction

Coronaviruses (CoV) belong to the family Coronaviridae, order Nidovirales. These viruses are divided into four genera: alpha, beta, gamma, and delta. Alpha, beta, and delta CoV affect mammals. However, all of them can move to different species, resulting in severe respiratory syndromes in humans, such as Middle East Respiratory Syndrome (MERS) caused by MERS-CoV, Severe Acute Respiratory Syndrome (SARS) caused by SARS-CoV, and recently also COVID-19, caused by SARS-CoV-2 (Fang Li, 2016). SARS-CoV-2 was first described in Wuhan, China in December 2019. In a few months, it spread to almost every country in the world, causing significant negative economic and social consequences, as well as causing a huge number of deaths and irreparable damage to the health of millions of people (Wei-jie Guan et al., 2020). As of May 30, 2022, 528,729,306 cases of SARS-CoV-2 infection and 6,287,340 deaths were registered in the world (Johns Hopkins Coronavirus Resource Center [JHCRC], 2022).

The coronavirus disease 2019 (COVID-19) includes a wide range of clinical manifestations, ranging from a completely asymptomatic course to multiorgan failure (Amanda Zakeri, Ashutosh P Jadhav, Bruce A Sullenger & Shahid M Nimjee, 2021). This is due to the different expression of angiotensin-converting enzyme 2 (ACE2) receptors on the surface of endothelial cells. Apoptosis and cell damage are the main consequences of the infection of vascular endotheliocytes. In addition to direct viral infection, destabilization of ACE2 induced by spike-binding glycoprotein (protein S), causes uncontrolled activation of the renin-angiotensin system, which also contributes to endothelial dysfunction (Aldo Bonaventura et al., 2021). A subsequent inflammatory response to exacerbation of pre-existing endothelial dysfunction may explain different susceptibility to viral infection among patients who are in the risk group of CVD (Istituto Superiore di Sanità [ISS], 2021). In patients with cerebrovascular pathology, the risk of mortality from COVID-19 increases, due to previously identified other risk factors, such as arterial hypertension, diabetes, hyperlipidemia, smoking, or stroke in anamnesis (Huijuan Jin et al., 2019). Neurological complications associated with COVID-19 occur in a significant proportion of patients. Data from a population-based follow-up study based in Wuhan, China, indicate that neurological abnormalities occur in 36.4% of hospitalized patients (Ling Mao et al., 2020). It could be that this number may vary depending on several factors: clinical conditions (ambulatory versus inpatient), demographic characteristics (age, gender, and ethnicity), and the method of neurological assessment (Samuel J Pleasure, Ari J Green & S Andrew Josephson, 2020). The mechanism of neurological changes that occur under the impact of COVID-19 remains to be determined, but it is probable to be heterogeneous and multifactorial, including direct damage of the brain by SARS-CoV-2, autoimmune factors, the occurrence of inflammation ("cytokine storm"), side effects from the use of drugs and metabolic disorders (Stella M Papa et al., 2020). In patients with neurological complications, disorders of liver enzymes synthesis, hemoglobin, lactate dehydrogenase (LDH), D-dimer, and lymphopenia are more often observed (Ling Mao et al., 2020). Thus, in our study of a single case of a complication that occurred after coronavirus infection, we would like to demonstrate the negative impact of the infection on the state of the vascular wall and the consequences it leads to.

Aim

To demonstrate that the comorbid disease of the cardiovascular system caused by coronavirus infection worsens the course of the initial manifestations of cerebrovascular insufficiency.

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Materials

A 63-year-old patient T., who suffered a coronavirus infection in October 2020 with respiratory symptoms, an increased body temperature (T=38°-39°C), and general weakness that lasted 20 days, has been examined in the neurological department of the State Institution «Head medical center of the Ministry of Internal Affairs of Ukraine» in December-January 2020-2021. The patient visited a polyclinic neurologist after she had recovered from COVID-19. She had complaints of a worsening condition. The patient had persistent attacks of headache, dizziness, and increased blood pressure (BP) up to 160/90 mm Hg. The polyclinic neurologist formulated a diagnosis: initial manifestations of cerebral blood circulation insufficiency. Arterial hypertension.

The patient underwent additional examination: general blood count, biochemical blood test, Doppler ultrasound of the main arteries of the head, ultrasound of the heart, and ECG at the polyclinic.

Anamnesis of the disease: by October 2020, the patient was diagnosed with autonomic dysfunction. The patient had seizures with an increased BP up to 150-160/90 mm Hg when she was suffering from COVID-19. A diagnosis of arterial hypertension was established after a consultation with a district therapist. D-dimer levels were the following: 1.6 (October 2020), and 1.2 (November 2020). Since October 2020, the following drugs have been prescribed: Xarelto 20 mg/day in the evening, Enalapril 5 mg 2 times a day in the morning and the evening, and Bisoprolol 5 mg once a day in the morning for constant use. After recovery from COVID-19, in 1.5-2 months, the patient began to suffer from attacks with palpitations, pulse acceleration up to 150 beats per minute, a feeling of fear and internal trembling with a slight increase in body temperature, and urination of significant amount of light urine after the attack. Attacks occurred 1-2-3 times a week for 2.5 months.

In December 2020, the patient was hospitalized at the neurological department of the State Institution «Head medical center of the Ministry of Internal Affairs of Ukraine», where a neurological status examination, a general blood count, a biochemical blood test, determination of the thyroid hormones' levels, ECG, Doppler ultrasound of the main arteries of the head and an ultrasound of the heart were performed.

Neurological status: productive contact is preserved. Meningeal signs are absent. Eye fissures D=S, pupils D=S, pupillary reactions are preserved, facial asymmetry is not detected, and tongue deviation is absent. Sensitive disorders were not detected. Tendon reflexes are symmetrical on both sides, muscle tone was not changed. Proboscis reflex was found, and Marinescu-Radovici and Strumpell reflexes were positive on both sides. Lability of the autonomic nervous system in the form of acrohyperthermia, eyelids, and fingers of outstretched hands tremor, slight unsteadiness in Romberg's position.

Results of laboratory and instrumental examination (December-January 2020-2021 during an examination at the State Institution «Head medical center of the Ministry of Internal Affairs of Ukraine»):

General blood count: erythrocytes $4.62 \cdot 10^{12}$/l; leukocytes $8.68 \cdot 10^{9}$/l; lymphocytes 41.4%; hemoglobin 140 g/l; platelets $226 \cdot 10^{9}$/l; ESR 24 mm/h.

Biochemical analysis of blood: glucose 5.62 mmol/l; cholesterol 5.91 mmol/l; triglycerides 1.97 mmol/l; creatinine 75 μmol/l; ALT 26 u/l; AST 27 u/l; HDL 1.4 mmol/l; LDL 4.23 mmol/l; coefficient of atherogenicity 3.22 u.

D-dimer: 0.8 (December 2020), 0.4 (January 2021).

Determination of the level of thyroid hormones: thyroid-stimulating hormone 1.59 μIU/ml.

Doppler ultrasound of the main arteries of the head: the thickness of intima-media complex (IMT) of the right common carotid artery in the middle third - up to 0.85 mm (normal rate up to 1.0 mm), in the bifurcation up to 1.04 mm (normal rate up to 1.1 mm), with partially lost differentiation into layers, echogenicity is not changed. The IMT of the left common carotid artery in the middle third is up to 0.91 (normal rate up to 1.0 mm), in the bifurcation, it has a local thickening up to 1.27 (normal rate up to 1.1 mm), with partially lost differentiation into layers, echogenicity is not changed.

Heart ultrasound: the cavity of the left ventricle is not expanded; the walls are not thickened. The global contractility of the left ventricle is within normal rates. Segmental contractility of the myocardium is not disturbed, normokinesia. Left ventricular diastolic dysfunction – delayed relaxation. The sizes and volumes of the heart cavities are within the normative range. Sealing of the front

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leaflet of the mitral valve is noted. A Doppler study of transmitral blood flow reveals mitral valve insufficiency of the 1st-2nd degree (regurgitation gradient of 49 mm Hg) - negative dynamics. The aortic valve has a classic structure. Sealing of all leaflets of the aortic valve is noted. Hemodynamics on the aortic valve is not disturbed. The aorta at the level of the valves of Valsalva and in the initial section of the ascending section is not dilated. The echo structure of the leaflets of the tricuspid valve is not changed. The main trunk of the pulmonary artery is not expanded, and the bifurcation has a classic structure. Hemodynamics on the valve of the pulmonary artery is not affected. No abnormalities in the echostructure of the pericardium were found. Echographic signs of pulmonary hypertension of the 1st degree (pressure in the pulmonary artery 25-50 mm Hg), without dynamics.

ECG: Heart rate 81 beats per minute. The electrical axis of the heart is 67°, a normal position. Sinus rhythm. Two-phase P-teeth: II. AVF. Two-phase T-teeth: V4. ST segment displacement: II, III, AVF (+), AVR (-).

Elevation: 0.12/0.15 (II), 0.10/0.11 (AVF), 0.11/0.09 (III);

Depression: - 0.07/-0.13 (AVR).

After the examination, a diagnosis was established: initial manifestations of cerebral blood circulation insufficiency, a paroxysmal course in the form of sympathoadrenal attacks with panic attacks. Arterial hypertension.

In the neurological department, the patient was prescribed: Platyfilin hydrotartrate 0.2%-1.0 subcutaneously No. 10 once a day, Armadin 2.0 intramuscular No. 10 once a day, after finishing injections, Armadin 100 mg, 1 tablet 3 times a day (within one month); Garlic (1200 units) once a day in the evening for 6 months, Bifren 250 mg 1 tablet twice a day (within one month).

After finishing taking medicine that was prescribed in the neurological department, from February 2021, the following medication was recommended for outpatient treatment: Mildronat 500 mg 1 capsule once a day (within a month), Adaptol 500 mg 1 tablet 2 times a day in the morning and the evening (for one and a half months).

The number of sympathoadrenal attacks with panic attacks after six months of treatment decreased to one per three months.

Coagulation tests were performed periodically and test results were the following: APTT – 37.7 sec., fibrinogen – 307 mg/dl (at the beginning of February 2021), APTT – 38.3 sec., fibrinogen – 3,1 g/l, PT – 11.1 sec., INR – 1.08, TT – 17.4 sec (in the middle part of February 2021), INR 0.98 (June 2021). The level of D-dimer was controlled regularly and registered at 0.2 from February to June.

From August 2021, after a course of treatment in the hospital, monitoring of biochemical blood analysis, ECG, and Doppler ultrasound of the main arteries of the head were performed on an outpatient basis.

Biochemical blood analysis: glucose 5.0 mmol/l; cholesterol 5.69 mmol/l; triglycerides 1.59 mmol/l; creatinine 73 μmol/l; ALT 22 u/l; AST 24 u/l; HDL 1.8 mmol/l; LDL 4.12 mmol/l; coefficient of atherogenicity 3.0 units.

ECG: a study without significant changes.

Doppler ultrasound of the main arteries of the head: IMT of the right common carotid artery in the middle third up to 0.65 mm (normal rate up to 1.0 mm), in the bifurcation up to 1.1 mm (normal rate up to 1.1 mm), with partially lost differentiation into layers, echogenicity is not changed. IMT of the left common carotid artery in the middle third is up to 0.76 (normal rate up to 1.0 mm), in the bifurcation, it has a local thickening up to 1.27 (normal rate up to 1.1 mm), with partially lost differentiation into layers, echogenicity is increased.

Outpatient treatment was continued from August 2021: Garlic (1200 units) 1 time a day in the evening for 6 months, Mildronat 500 mg 1 time a day (for a month), Adaptol 500 mg 1 tablet 2 times a day in the morning and the evening (for one and a half months); the dose of Xarelto reduced to 15 mg/day.

The patient's coagulation tests were under monitoring. The results were the following: PT – 13.2 sec., INR – 1.18, APTT – 37.2 sec., TT – 16.3 sec. (September 2021), D-dimer - < 0.5, PT– 11.7 sec., INR – 1.04, APTT – 28 sec., TT – 17 sec., fibrinogen – 3.7 g/l (November 2021), PT– 12.2 sec., INR – 1, APTT – 24 sec., TT – 16.1 sec., fibrinogen – 3.3 (August 2022).

Results

The coronavirus infection in our patient affected the deterioration of the cerebral vessels functioning, specifically, the increasing of the initial manifestations of cerebral blood circulation insufficiency, to which arterial hypertension was added, and over time sympathoadrenal attacks

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with panic attacks. In our patient, the increase in blood pressure occurred without sympathoadrenal attacks. This is due to the interaction between the spike-binding glycoprotein (protein S) of the virus and angiotensin-converting enzyme 2 (ACE2) receptors on the surface of endothelial cells. In addition to direct viral infection, destabilization of ACE2 caused uncontrolled activation of the renin-angiotensin system, which also leads to endothelial dysfunction and increased blood pressure (Aldo Bonaventura et al., 2021). Further exacerbation of pre-existing endothelial dysfunction explains the different susceptibility to viral infection in patients with a predisposition to cardiovascular diseases such as hypertension (Istituto Superiore di Sanità [ISS], 2021). The last provokes a complication associated with irritation of the suprasegmental part of the autonomic nervous system, namely the posterior part of the hypothalamus, which leads to the development of sympathoadrenal attacks with panic attacks. Irritation of the suprasegmental part of the autonomic nervous system is caused not only by changes in vascular tone under conditions of increased blood pressure but also by dysfunction of the vascular walls under the influence of a viral infection, which contributes to increasing IMT.

The increase of IMT is the result of the growth in the number of monocytes-phagocytes with modified low-density lipoproteins (m-LDL), which turn into foam cells that are the basis of atherosclerotic plaques. To a certain extent, a "vicious circle" is formed, which we must destroy through performing the treatment. Under the influence of statins (garlic amino acids isolated from garlic have the properties of statin drugs), scavenger receptors of monocytes are blocked, the number of which on the surface of cells is stimulated by viruses in the presence of infection, and right to them LDL are attached. Blocking the capture of LDL by phagocytes limits the formation of foam cells, which are the basis of atherosclerotic plaques, and leads to IMT decreasing, as happened in our patient. According to the results of an ultrasound examination of the main arteries of the head, after six months of using Garlic, the IMT of the left common carotid artery decreased by 0.15 mm - from 0.91 mm (registered in December 2020) to 0.76 mm (registered in June 2021), and IMT of the right common carotid artery by 0. 2 mm - from 0.85 mm (registered in December 2020) to 0.65 mm (registered in June 2021). This is an indication of the positive effect of statin drugs on the IMT reducing with subsequent improvement of the function of vascular walls. Under the influence of the use of statin, sedative, and nootropic drugs in our patient, the irritation of the posterior part of the hypothalamus and the number of sympathoadrenal attacks decreased from 1-2-3 per week to 1 within 3 months after the first 3 months of inpatient and outpatient treatment, and six months after the outpatient treatment - up to 1 within 6 months. Our patient's general condition improved: the headache attacks with dizziness disappeared and blood pressure stabilized in the range of 120-125/80 mm Hg under the influence of antihypertensive drugs. Thus, it can be stated that arterial hypertension developed after the coronavirus infection in patient T. could lead to the deterioration of the course of the initial manifestations of cerebral blood circulation insufficiency with the subsequent development of sympathoadrenal attacks with panic attacks. For further conclusions, it is necessary to continue our studies with a larger number of patients.

Conclusions

A combination of coronavirus infection and arterial hypertension may lead to the worsening of the course of such slowly progressing disorders of cerebral blood circulation as the initial manifestations of cerebral blood circulation insufficiency with the development of sympathoadrenal paroxysms with panic attacks.

Treatment with statins, anticoagulants, antihypertensive, nootropic, and sedative drugs helps to stabilize arterial hypertension and reduce the number of sympathoadrenal attacks with panic attacks in patients.

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Conflict of interest

The authors declare no conflict of interest.

Consent for publication

All authors have read the text of the manuscript and given their consent for its publication.

Consent for publication: informed consent was obtained from the patient.

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Клінічний випадок перенесеної коронавірусної інфекції із ускладненням

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Анотація: коронавірусна інфекція, збудник SARS-CoV-2, здатна викликати широкий спектр клінічних проявів. Особливу небезпеку дана інфекція несе для пацієнтів зі схильністю до серцево-судинних захворювань, таких як гіпертонія. Зміни судинного тонусу за умов підвищення артеріального тиску, а також дисфункція судинних стінок під впливом вірусної інфекції призводять до подразнення надсегментарного відділу автономної нервової системи, а саме задньої частини гіпоталамусу, що провокує розвиток симпато-адреналових нападів із панічними атаками. Метою даної роботи було продемонструвати, що коморбідне захворювання серце-

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во-судинної системи викликане після перенесеної коронавірусної інфекції погіршує перебіг початкових проявів недостатності мозкового кровообігу. У неврологічному відділенні ДУ «Головний медичний центр Міністерства внутрішніх справ України» в грудні-січні 2020-2021 року була обстежена пацієнтка Т., 63 років, яка в жовтні 2020 року перенесла COVID-19. При оцінці неврологічного статусу пацієнтки було виявлено позитивні патологічні рефлекси: хоботковий та рефлекс Марінеску-Радовичі, стопний патологічний розгинальний рефлекс Штрюмпелля з двох боків та лабільність вегетативної нервової системи у вигляді акрогіпертермії, тремору повік та пальців витягнутих рук, незначної хиткості в позі Ромберга. Пацієнтці було проведено загальний аналіз крові, біохімічний аналіз крові, ультразвукову доплерографію магістральних артерій голови (УЗДГ МАГ), ультразвукову діагностику серця (УЗД серця), електрокардіографію (ЕКГ). Особливу увагу варто приділити результатам УЗДГ МАГ: комплекс інтима-медіа (КІМ) лівої загальної сонної артерії в середній третині товщиною до 0,91, в біфуркації має локальне потовщення до 1,27, правої загальної сонної артерії в середній третині товщиною до 0,85 мм (норма до 1,0 мм), в біфуркації товщиною до 1,04 мм (норма до 1,1 мм), з частково втраченим диференціюванням на шари, ехогенність не змінена. Завдяки проведеному лікуванню пацієнтки із застосуванням препаратів групи статинів блокуються скавенджер-рецептори моноцитів, кількість яких на поверхні клітин стимулюється вірусами за наявності інфекції і саме до них приєднуються ЛПНЩ. Блокування захвату ЛПНЩ фагоцитами, обмежує утворення пінистих клітин, які лежать в основі атеросклеротичних бляшок і призводить до зменшення товщини КІМ. За результатами УЗДГ МАГ у нашої пацієнтки за півроку проведеного лікування товщина КІМ лівої загальної сонної артерії зменшилась від 0,91 мм до 0,76 мм, правої - від 0,85 до 0,65 мм. Поєднання коронавірусної інфекції та артеріальної гіпертензії може погіршувати перебіг таких повільно прогресуючих порушень мозкового кровообігу, як початкові прояви недостатності мозкового кровообігу з розвитком симпато-адреналових пароксизмів із панічними атаками. Проведене лікування із застосуванням статинів, антикоагулянтів, гіпотензивних, β-блокаторів, ноотропних та седативних препаратів сприяє стабілізації артеріальної гіпертензії та зменшенню кількості симпато-адреналових нападів з панічними атаками в пацієнтів.

Ключові слова. COVID-19, гіпертензія, панічні атаки, потовщення каротидного комплексу інтима-медіа, симпато-адреналова система.