CHAPTER

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Prognosis of stroke in a patient with SARS-CoV-2 and coronary artery bypass graft surgery

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ABSTRACT
Objective: To report a case of a patient with ischemic stroke, previous coronary artery bypass graft surgery (CABG), and cardiovascular and endocrine-metabolic comorbidities associated with complications from SARS-CoV-2. Case details: A 75-year-old patient was admitted to a referral hospital in Brasilia/Federal District in June 2020 due to sudden loss of consciousness, hemiparesis in the right dimidium, and aphasia with conjugated ocular deviation for 1 hour. He has coronary artery disease with coronary artery bypass graft surgery 3 years ago, arterial hypertension, chronic kidney disease stage IV by the Chronic Kidney Disease Epidemiology Collaboration, hypothyroidism, metabolic syndrome, and obstructive sleep apnea syndrome. During hospitalization, RT-PCR was performed with the detection of the RNA of SARS-CoV-2 and chest CT showing opacities with ground-glass attenuation and inflammatory bronchopathy. Final considerations: In the presence of coronavirus, ischemic stroke occurs in the most severe cases of the disease, due to the neurotropism of the virus and the complications of the patient with cardiovascular comorbidities. Coronary artery bypass graft surgery represents a worse prognosis factor when in the immediate postoperative period in these patients with a high mortality rate. However, in the present case, the patient with a history of CABG had a favorable clinical outcome.

Keywords: SARS-CoV-2, stroke, myocardial revascularization.

1 INTODUCTION

SARS-CoV-2 is a betacoronavirus that causes the disease COVID-19. According to the World Health Organization (WHO), globally, in October 2020, 33,722,075 confirmed cases were registered, of which 1,009,270 deaths. The disease is usually mild, with the most characteristic symptoms being fever, dry cough, and tiredness. However, it is still possible to find in patients: dyspnea, chest pain, headache, diarrhea, anosmia, ageusia, and skin eruptions.

In addition, severe cases that required follow-up in intensive care units were accompanied by other comorbidities such as hypertension, cardiovascular diseases, stroke, chronic kidney disease (CKD), diabetes, and lung diseases (WORLD HEALTH ORGANIZATION, 2020; WHITTAKER A, et al., 2020; MONTALVAN V, et al., 2020).

The virus responsible for the current pandemic, SARS-CoV-2, acts similarly to the SARS-CoV that emerged in mid-2002. The current betacoronavirus binds to the angiotensin-converting enzyme 2 (ACE2) receptor as did its predecessor. This receptor is found in several cells of the human body, such as endothelial cells, muscle cells of the tunica intima and media of the muscular arteries of the brain, glial cells and neurons. This finding demonstrates the potential neurotropic involvement of SARS-CoV-2, indicating the possible severity of the disease (ZHOU Z, et al., 2020; WHITTAKER A, et al., 2020).

The name “coronavirus” arose due to the crown shape that the encapsulated virus presents, when observed under electron microscopy. This crown is made up of membranous glycoproteins in a spiculated shape. Furthermore, the betacoronavirus contains genetic material consisting of a single strand of RNA, being considered one of the largest genomes of its group.

Coronaviruses belong to the domain Riboviria, kingdom Orthornavirae, phylum Pisuviricota, class Pisoniviricetes, order Nidovirales, family Coronaviridae, and subfamily Orthocoronavirinae. This subfamily is divided into four genera: Alphacoronavirus, Betacoronavirus, Gammacoronavirus and Deltacoronavirus. Alphacoronavirus possesses species HCoV-229E, HCoV-NL63 and Mi-BatCoV 1A. Betacoronavirus includes, among others, HCoV-OC43, HCoV-HKU1, MERS-CoV, SARS-CoV and SARS-CoV-2. Gammacoronavirus has IBV, TCoV and BWCoV-SW1 as examples. The Deltacoronavirus, in turn, presents, among others: BuCoV HKU11, WiCoV HKU20 and ThCoV HKU12 (WOO PCY, et al., 2012; CAROD-ARTAL FJ, 2020; BERGER JR, 2020).

There are dozens of studied coronaviruses, but only seven species have been proven to infect humans: MERS-CoV, SARS-CoV, HCoV-HKU1, HCoV-OC43, HCoV-229E, HCoV-NL63, and, finally, the current SARS- CoV-2. This has emerged in recent months, due to the excellent mutation capacity shown by the coronaviruses, even allowing its transmission among many species of mammals and birds (CAROD-ARTAL FJ, 2020).

Despite being the most common, the respiratory system (RS) is not the only gateway for COVID-19 in humans. Many reports in the scientific literature suggest the invasion of the virus through the gastrointestinal tract. This theory is supported by the clinical picture of many patients, associated not only with respiratory signs and symptoms but also with gastroenterological ones. Even though the mechanical process was initiated in the nasopharyngeal mucosa, it continues through the SR and/or gastrointestinal tract and, in response to the neurotropism of SARS-CoV-2, can even enter the patient's central nervous system (CNS).

The virus repeatedly manipulates the lymphatic, vascular, and even nervous systems, notably the enteric system, to work the CNS to its advantage. In this way, the betacoronavirus can cause stroke following several mechanisms: vascular involvement, with inflammation of its walls; hypercoagulability; myocardial injury; release of atherosclerotic plaques from their formation site, blocking blood flow to the brain, leading to tissue necrosis, among others (BOSTANCIJKLIJOGLU M, 2020; TREJO-GABRIEL-GALÁN JM, 2020).

According to Barrios-López JM, et al. (2020) and Trejo-Gabriel-Galán JM (2020), many neurological disorders were analyzed in patients with COVID-19. Among them, the ischemic stroke category was identified in 2-3% of patients hospitalized in the city of Wuhan, China. There was even an increase of 5-6% in the incidence of stroke in patients who expressed severe disease. Hypercoagulability associated with high levels of D-dimer attached to the outbreak of systemic inflammation confirmed by laboratory tests is a strong indication of stroke in these patients. Stroke can be divided into ischemic and hemorrhagic. The former is more common, accounting for approximately 70% of strokes worldwide. The second covers hemorrhage with an intracerebral focus and hemorrhage with a subarachnoid focus. With the technological development of medicine, the diagnosis of stroke had increased in its classification. More sophisticated imaging exams allowed a better stratification of stroke based on deeper studies of tissue lesions. When these injuries are not permanent, it is called a transient ischemic attack. When permanent, stroke is diagnosed (CAMPBELL BCV, et al., 2019).

The present work aimed to narrate a case of a patient with a stroke due to complications caused by the betacoronavirus. The study also presented relevant particularities for the unfolding of the pathophysiology of SARS-CoV-2 in the patient, such as cardiovascular, endocrine-metabolic comorbidities, obesity, history of smoking with a smoking history of 30 packs/year, and senility. In addition, the patient had had coronary artery bypass grafting (CABG) relatively recently (3 years ago), due to coronary artery disease (CAD), which justified the study and publication of the case in the scientific literature.

2 CASE DETAILS

A.I.P., male, 75 years old, was admitted to a reference hospital in Brasília/DF in June 2020 with a history of an episode of a sudden loss of consciousness followed by hemiparesis in the right side of the body and aphasia with conjugate ocular deviation for 1 hour. Computed tomography (CT) of the skull without contrast was performed, which ruled out ischemic or hemorrhagic lesions on admission.

Patient with a previous pathological history of CAD with CABG for 3 years, hypertension, CKD stage IV by the Chronic Kidney Disease Epidemiology Collaboration, hypothyroidism, metabolic syndrome, obstructive sleep apnea syndrome, hiatal hernia, and former smoker, with a smoking history of 30 packs/year (UTIEL FJB, et al., 2020).

Upon admission, a diagnostic hypothesis of ischemic stroke and complications of CKD stage IV with atrial fibrillation questioned was raised. The patient reported continuous use of a platelet antiaggregant, beta-blocker, loop diuretic, statin, synthetic thyroid hormone, and xanthine oxidase inhibitor.

On examination, he was in regular general condition, drowsy, anicteric, cyanotic, feverish to the touch, pale, dehydrated, and eupneic with ventilatory support from a nasal catheter 5L/min. The cardiovascular system is uneventful with a blood pressure of 96x72 mmHg and a heart rate of 84 bpm. RS with diffuse reduction of physiological breath sounds, without adventitious sounds. Abdomen globular, distended, hyper tympanic, without visceromegaly, painless on superficial and deep palpation, present bowel sounds, and no signs of peritoneal irritation. Bilateral symmetric pedal and popliteal pulses with mild edema and hemiplegia on the right side of the body. He had aphasia with involvement in the Wernick and Broca areas.

After a week of hospitalization, the patient remained drowsy, with global aphasia, and using a nasoenteric tube since admission. A new brain CT without contrast showed a hypoattenuating area with involvement of the territory of the left middle cerebral artery (ACME), which presented difficulty in the irrigation of the frontal and parietal lobes, in addition to the insula, internal capsule, caudate and lentiform nuclei, striatum and part of the globe pale.

Effacement of the grooves in the cortical gyri was visualized. Presence of slight compression of the lateral ventricle and contralateral midline deviation of approximately 4 mm. Left brainstem with hypoattenuation. No signs of extra-axial collections or foci of intraparenchymal hemorrhage. Other anatomy-physiological findings on CT of the head were unchanged. With a conclusive report for acute/subacute ischemic stroke in the territory of the ACME, the patient still developed a productive cough, restless sleep, and the need for increased ventilatory support.

Laboratory tests showed sodium 130.7 mmol/L; potassium 6.3 mmol/L; chlorine 94 mmol/L; serum glucose 202 mg/dL; creatinine 2.26 mg/dL; urea 137.1 mg/dL; amylase 187 U/L; total bilirubin 0.33 mg/dL; direct bilirubin 0.04 mg/dL; indirect bilirubin 0.29 mg/dL; magnesium 2.7 mg/dL; total protein 6.0 g/dL; albumin 4.0 g/dL; globulin 2.0 g/dL; TGO 47 U/L; red blood cells 5.81 million/μL; hemoglobin 17.1 g/dL; hematocrit 52.4%; leukocytes 7,100/μL; neutrophils 82.3%; eosinophils 0%; basophils 0.9%; monocytes 8.9%; lymphocytes 7.8% and platelets 200,000/μL.

This allows us to infer the need to correct the hydro electrolyte disturbances presented with intravenous sodium replacement therapy due to its depletion, in addition to potassium restriction in the diet and increased elimination with loop diuretics administered orally. About high serum glycemia, and depending on the diabetes mellitus previously identified in the patient, therapy with an insulin analog is proposed to resolve the condition in question.

Due to the worsening of the clinical respiratory condition, in July 2020, a chest CT without contrast was performed, which showed opacities with ground-glass attenuation and bilateral intralobular lines of predominantly peripheral distribution. Pulmonary involvement is approximately

60%. Thickened-walled bronchi inferring inflammatory bronchopathy. Soon after, the Polymerase Chain Reaction with Reverse Transcription (RT-PCR) test was performed, being detectable for the RNA of SARS-COV-2, confirming the presence of the coronavirus infection.

The patient then underwent treatment for COVID-19 for 21 days until clinical improvement. Laboratory tests gradually improved with the reversal of sodium depletion and readjustment of potassium. Due to acute renal failure with elevated urea and creatinine levels, the patient underwent hemodialysis until renal function was restored. There was a slight improvement in neurological function. The patient evolved with hemodynamic stability, without the need for vasoactive drugs and signs of respiratory distress. On physical examination, he was lucid and oriented in time and space, cooperative to commands, with preserved physiological diuresis and evacuation. Despite the comorbidities presented by the patient, he had a good response to the proposed treatment and was discharged in August 2020.

3 DISCUSSIONS

According to Morassi M, et al. (2020), stroke is not a common finding in patients infected with SARS-CoV-2. However, when diagnosed, it can determine an unfavorable prognosis. The patient in the present study has several cardiovascular comorbidities and a relatively recent history of CABG, which, together, define a negative prognosis in the fight against COVID-19.

Yaghi S, et al. (2020), corroborate in their studies, the incidence of ischemic stroke of 0.9% in a total of 3556 patients. While Barrios-López JM, et al. (2020) and Trejo-Gabriel-Galán JM (2020) determine a greater appearance of ischemic stroke as complications of the coronavirus. According to both authors, 2.8% of patients diagnosed with COVID-19 evolved with stroke and this number is even higher (5.7%) in patients with comorbidities. It is important to emphasize the association of stroke with high D-dimer rates.

Despite reports of ischemic stroke in young people affected by SARS-CoV-2, the highest prevalence is still found in the elderly. The average was 71 years. COVID-19 was more deleterious in patients who previously had hypertension, dyslipidemia, diabetes mellitus, asthma, and cardiovascular and cerebrovascular diseases. The pathophysiology of the disease is correlated with inflammation and coagulation disorders, which justifies ischemic stroke (AVULA A, et al., 2020).

González-Pinto T, et al., (2020) also ratify the damage caused by SARS-CoV-2 in extending the prothrombin time, systemic inflammation, hypercoagulability, thrombocytopenia and increased risk for disseminated intravascular coagulation.

In the case reported in this study, the patient had cardiovascular, endocrine-metabolic and neurological comorbidities upon admission. The ischemic stroke led the patient to Wernick and

Broca's aphasia associated with dysarthria and hemiparesis of the right side of the body. After a week of hospitalization, the patient developed desaturation requiring ventilatory support. Non-contrast-enhanced chest CT scans have reported ground-glass opacities in approximately 60% of the lung parenchyma and significant inflammatory bronchopathy.

It was not possible to confirm anosmia or ageusia due to the clinical picture of the patient. However, as determined by the literature, the SR and CNS suffered significant injuries due to the pathophysiology of SARS-CoV-2. Patients often report headache, dizziness, ageusia, hypogeusia, anosmia, hyposmia, and disturbances of consciousness, due to the neurotropism of COVID-19 (HESS DC, et al., 2020; MONTALVAN V, et al., 2020).

The pathophysiology of SARS-CoV-2 permeates the panorama of myocardial, renal or pulmonary lesions, cardiac arrhythmias, coagulation disorders and their respective consequences. When related to surgical procedures, the coronavirus played a relevant role in the clinical outcome of patients. In a study carried out in Wuhan, China, 100% of patients had pneumonia, 44% required intensive care, 32% developed acute respiratory distress syndrome and 21% of patients died (PATEL V, et al., 2020).

Betacoronavirus is formed externally by a spiculated glycoprotein crown. These spikes are polypeptide chains that bind to cell receptors in the human body. This union is mediated by ACE2 located on the surfaces of these cells. SARS-CoV-2 is 100-150 nanometers in size and have positive single-stranded RNA. ACE2 receptors have a high affinity for the polypeptide spikes of coronaviruses. These receptors are abundant in the CNS, more specifically, in the ventrolateral side of the reticular formation and the nucleus of the solitary tract, both located in the medulla oblongata in the brainstem. In this region are neuronal clusters responsible for cardiovascular and respiratory function (MONTALVAN V, et al., 2020; BERGER JR, 2020).

Yandrapalli S, et al. (2020) reported an unfavorable prognosis for patients with COVID-19 and in the postoperative period of CABG. In the study, the patient developed hypoxia and fever on the first postoperative day (POD). In chest CT, came the report of bilateral consolidation and, in the RT-PCR study, detection of SARS-CoV-2. Sometime later, death from severe pneumonia. The authors also refer to other types of surgeries with a high postoperative lethality rate. All with cardiorespiratory complications and multiple organ failure.

Rescigno G, et al. (2020) demonstrated in a study an obese and chronic alcoholic patient in need of CABG due to unstable angina, unchanged troponin and cardiac catheterization indicating CAD with stenosis of the left main coronary artery. Prior stroke without sequelae. Despite successful surgery and echocardiogram without residual tricuspid regurgitation, the patient evolved with hypoxia, dyspnea and fever. Chest CT showed bilateral consolidation. Echocardiogram indicated left ventricle functions adequately, despite considerable damage to the right ventricle. The ventilatory pattern worsened with death on the ninth POD. The authors show growing concern with urgent surgical treatments in patients with COVID-19, due to frequently unfavorable clinical outcomes, especially in cardiovascular surgeries.

In the current study, it was observed that the CABG was performed 3 years ago. The patient still had cardiovascular and endocrine-metabolic comorbidities and was admitted to the hospital with ischemic stroke and subsequent COVID-19 with a report established by RT-PCR and chest CT. However, the patient's clinical outcome was favorable, with a good response to the proposed treatment and medical discharge on August 28, 2020.

When a patient is admitted to the hospital with an ischemic stroke, the recommended treatment is intravenous thrombolysis or, in more specific cases, endovascular thrombectomy. Thrombolytic medication is designed to dissolve the clot that is obstructing blood flow. The ideal time for administering the drug is up to 4.5 hours. However, there are reports in the literature of benefits up to 9 hours after the stroke. Thrombectomy, as well as thrombolysis, are more effective the faster the treatment is started, being one of the determining factors for a good prognosis (CAMPBELL BCV, et al., 2019).

It can be concluded from the versed case report that the pathophysiology concerning the cardiorespiratory and neurological manifestations of COVID-19 still needs to be studied. Many studies published in the literature corroborate the neurotropism of SARS-CoV-2 and its complications, especially in patients with comorbidities. However, there is still much to be clarified about the pathological changes caused in the cells and tissues of patients affected by the disease.

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