COVID-19 AND PULMONARY THROMBOEMBOLISM: A CASE REPORT

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Abstract

COVID-19 is an acute viral infection caused by SARS-CoV-2 coronavirus. This pandemic disease stands out for the marked variation in the clinical characteristics of patients, ranging from asymptomatic cases to severe organ dysfunction and death. Serious complications occur in the late phase of the disease or even after viral infection, and thrombotic events are one of these complications. In this context, this study aimed to report a case of an obese, young adult female patient with a complication of pulmonary thromboembolism after infection by COVID-19.

Keywords: SARS-CoV-2, pandemic disease, pulmonary thromboembolism

Introduction

The record of the first cases of infection of the new coronavirus in humans, whose scientific name is SARS-CoV-2, known as COVID-19, occurred in China on December 31, 2019 (CABRAL et al., 2020). The first record in Brazil occurred in February of the year following the Chinese case and the pandemic was only decreed in March 2020 (LARGURA, 2022).

Nationally, the COVID-19 pandemic has had one of the greatest negative impacts on public health in Brazilian history, as it has been marked by a rapid spread of the disease. However, epidemiological data from the World Health Organization (MATTA, 2021) has shown little about the transmission characteristics of COVID-19 in a context of social inequality, with populations living in precarious conditions of housing and sanitation, without systematic access to water, and a situation of population

agglomeration, characteristics that can favor contamination (LOANNIDIS, 2020).

Contagion of SARS-CoV-2 has an average incubation period that varies between 3 to 7 days. This contamination occurs through inhalation of respiratory droplets or through droplets of saliva that can become suspended in the air after sneezing, coughing, and sputum or due to close contact with sick individuals or contaminated surfaces (CASTRO, 2022). Thus, preventive measures are recommended for frequent hand hygiene with water, soap, gel alcohol, and the use of a mask covering the nose and mouth, without forgetting social distance, avoiding contact with the eyes, nose, and mouth of any individual.

Symptoms after contact with the virus, followed by infection with SARS-CoV-2, can be represented by fever, cough, coryza, odynophagia, headache, diarrhea, myalgia, anosmia, ageusia, dyspnea, and others, although some infected people have declared themselves asymptomatic (FRANCO, 2022). Also, patients with severe forms of the disease or patients associated with comorbidities will have a considerable increase in the negative prognosis of the disease (BRASIL, 2019). Importantly, complications such as viral and/or bacterial pneumonia, severe acute respiratory syndrome, acute kidney injury, pulmonary thromboembolism, acute myocardial infarction, and ischemic and hemorrhagic stroke may occur concomitant to the infection (FILHO, 2021).

Therefore, thrombotic events, standing out the pulmonary thromboembolism (PTE), are one of the common serious complications in the late phase of the disease or even after COVID-19. In this sense, the physician must pay attention to this possibility and advise the patient to seek medical attention if respiratory symptoms worsen after medical discharge. In this context, this study aimed to report the case of a patient without risk factors for thromboembolism post-COVID-19 and with evolution to PTE.

Case report

Patient M.I.S, 37 years old, female, personal history of asthma, obese, and positive for COVID-19 antigen on the fourth day of symptoms. The patient sought the Emergency Care Unit (UPA) on the sixth day after the onset of symptoms, which consisted of fever, coryza, myalgia, and persistent cough. Thus, the patient was medicated with systemic corticosteroids and intravenous hydration, being then discharged.

The patient returned to the Emergency Care Unit (UPA) on her tenth day of evolution, complaining of dyspnea, and being hospitalized in the unit's covid wing. The patient developed acute respiratory failure after a day of hospitalization, requiring orotracheal intubation, and being referred to the regional reference hospital. The patient suffered a cardiopulmonary arrest (CPA) during admission to the intensive care unit (ICU), being reversed after one cycle of cardiopulmonary resuscitation (CPR) maneuvers.

General physical examination: heart rate (HR): 80 bpm, O₂ saturation (SAT): 100%, orotracheal intubation (OTI): volume-controlled ventilation (VCV), positive end-expiratory pressure (PEEP): 14, fraction of inspired oxygen (FIO₂): 90%, tidal volume (TV): 400, and ventilation/perfusion (V/P): 95. Pulmonary auscultation showed reduced breath sounds globally, with crackles in the middle third and base of the lung bilaterally. Cardiovascular auscultation showed regular heart rhythm, without audible murmurs.

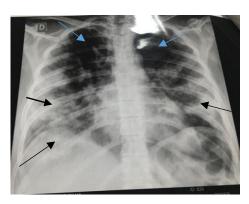


Figure 1. Chest X-ray on admission to the intensive care unit (ICU) of the patient with COVID-19. Black arrows indicate the presence of pulmonary infiltrate. Blue arrows indicate the existence of foci of bilateral pulmonary consolidations.

Chest radiography during ICU admission showed infiltrate (black arrow) and consolidation foci (blue arrow) bilaterally. Initially, computed tomography was not performed because of the patient's hemodynamic instability (Figure 1).

The patient was placed in the prone position during the fourteenth day of ICU stay due to respiratory worsening. A chest CT angiography was requested, which did not show signs of pulmonary thromboembolism and with consolidations and diffuse and bilateral ground-glass infiltrate, affecting more than 50% of the lung parenchyma. A small bilateral pleural effusion was also observed. The patient continued to use mechanical ventilation until the twenty-seventh day of hospitalization, being then extubated.

The patient did not need mechanical ventilation or vasoactive drugs on the thirtieth day and used supplemental oxygen through a nasal catheter at 5 liters per minute. Moreover, the patient was conscious and oriented, being discharged from the ICU to the ward.

The patient remained on the ward for 4 days, evolving with significant clinical improvement, including laboratory tests, and being discharged from the hospital without the use of supplemental O₂, saturating 93% on room air.

Subsequently, the patient came to the health unit 39 days after the first symptom, presenting a productive cough, epigastric pain associated with nausea and dysphagia, and burning retrosternal pain, with a total weight loss of 12 kg. Also, the patient was using apixaban 2.5 mg 12/12h for thrombosis prophylaxis.

General physical examination: saturation of 91% on room air. Respiratory auscultation showed bilateral vesicular murmur with diffuse wheezing and fine rales at the base bilaterally. Laboratory tests: hemoglobin: 15.3; hematocrit: 44.6; leukocytes: 9300; platelets: 346,000; creatinine: 0.4; C-reactive protein (CRP): 3.12; TGO: 33; TGP: 35; and CPK: 80.

After 50 days of evolution after COVID-19, the patient returned reporting a productive cough with worsening at night, a saturation of 94% on room air, in addition to frequent headache, nausea, and vomiting. A new chest CT angiography was then requested.

Chest CT angiography (Figure 2) showed the following findings: filling defects in segmental and subsegmental arterial branches to the posterior basal segment of the right lower lobe, inferring pulmonary thromboembolism (red arrow in Figure 2); nonspecific mediastinal lymph nodes enlarged in number, with

probable reactional nature; cardiac dimensions within the normal range; mild diffuse thickening of the bronchial walls of probable inflammatory nature; reticular and ground-glass opacities (yellow arrow in Figure 2), sometimes associated with interlobular septal thickening, foci of consolidation and traction bronchiectasis dispersed throughout both lungs, with pulmonary involvement higher than 50% (marked), probably related to late inflammatory changes after viral infection (COVID-19).

Full anticoagulation was then started with apixaban 10 mg 12/12 hours for 7 days, followed by 5 mg 12/12 hours for 6 months due to the diagnosis of acute PTE. At this time, the patient was hemodynamically stable (PESI + 10 points), without the need for hospital admission at the first moment.



Figure 2. Chest CT angiography of a patient affected by COVID-19. Red arrows indicate filling defects in segmental and subsegmental arterial branches to the posterior basal segment of the right lower lobe. Yellow arrows indicate reticular and ground-glass opacities.

Discussion

The unusual formation of blood clots is among the most worrisome complications in COVID-19, even in patients who were receiving prophylactic anticoagulation (SAÚDE, 2020). Thus, these patients have developed multiple comorbidities associated with infectious prevalence, and thrombosis is one of the major sources of secondary complications, according to this report.

This outcome (thrombosis) occurs due to exaggerated responses of the immune system to the virus, causing an increase in the levels of pro-inflammatory cytokines and chymosins (MARCONE & MARQUES, 2020). Thus, this imbalance leads to the formation of thrombi through pro-coagulant activities, in addition to impairing the functioning of the lungs and tissues due to the hypoxia process. This thrombus formation affects the circulation, generating clots, intensifying the immune response, and causing inflammation.

The patient presented criteria for using prophylactic anticoagulants during evolution. The severity criteria consisted of arterial oxygen saturation lower than 93%, PaO2/FiO2 lower than 300, and pulmonary

involvement higher than 50% of the lung parenchyma on radiology.

Among the Wells score criteria (stratification criteria based on signs and symptoms for PTE), the patient had only prolonged immobilization and tachycardia (3 points). Regarding the SIC (sepsis-induced coagulopathy) score, the platelets decreased below 100,000 or INR was higher than 1.4 seconds at no time during the patient's evolution.

Currently, there is still no evidence to indicate full therapeutic anticoagulation based only on isolated laboratory values, such as interleukin-6, D-dimer, ferritin, or coagulation tests such as PT, aPTT, and fibrinogen. In this context, the general clinical condition of the patient must also be considered (HANA H et al., 2020). Thus, it is suggested to stratify patients with COVID-19 infection according to the severity of the case.

In the patient, the therapeutic options described in the literature after clinical and imaging diagnoses (CT angiography) consist of starting full anticoagulation with low molecular weight heparin (LMWH) at a dose of 1 mg/kg twice a day subcutaneously or unfractionated heparin (UFH) intravenously in a continuous infusion pump (ZHAI Z et al., 2020; RODRIGUES, 2022).

Pádua and Caprini scores have been used to perform the risk stratification of pulmonary thromboembolism (PTE) in medical clinic and surgical patients and, currently, patients with COVID-19 (FARHAT F.G.L.C., 2018; LOBASTOV, 2020). Patients at high thrombotic risk should ideally receive pharmacological and mechanical prophylaxis. Patients at low and moderate risk for PTE should receive only pharmacological prophylaxis (ZHAI et al., 2020). Stratification for thrombotic risk for the institution of pharmacological prophylaxis for up to 7 days in cases considered to be at high risk for PTE should be considered in patients with mild conditions in quarantine or patients discharged from hospital (Rodrigues et al., 2020). All patients should be evaluated for risk of bleeding before administering anticoagulant therapy (GAGE et al., 2006).

Asymptomatic patients may have a condition of infection by the new coronavirus, with manifestations of signs and symptoms of venous thromboembolism. On the other hand, symptomatic patients may present progressive or sudden worsening when the thrombotic event is installed.

Conclusion

Pulmonary thromboembolism is one of the diseases related to COVID-19. Therefore, there is a need for more randomized trials on prophylaxis and appropriate antithrombotic treatment. Thus, risk stratification and individualized follow-up of the patient in the post-COVID-19 period, with anamnesis and clinical evaluation, in addition to complementary examinations, are necessary to avoid unfavorable evolutions.

References

Cabral, R.B.G. et al. **Estudo inicial sobre a evolução do novo CORONAVÍRUS (SARS-COV-2) no estado do Pará (Brasil), no período entre 17/03/2020 e 06/04/2020.** Brazilian Journal of Health Review, v. 3, n. 2, p. 2914-2931, 2020.

Largura, T. S. **Análise do impacto da pandemia de Covid-19 no setor de comércio em Santa**International Educative Research Foundation and Publisher © 2022 pg. 172

Catarina. TCC (graduação) - Universidade Federal de Santa Catarina. Centro Sócio-Econômico. Economia, 2022.

Ioannidis J.P.A., Coronavirus disease 2019: the harms of exaggerated information and nonevidence-based measures. Eur J Clin Invest, v. 50, e: 13222, 2020.

Matta, G.C., Rego, S., Souto, E.P., And Segata, J., Eds. **Os impactos sociais da Covid-19 no Brasil: populações vulnerabilizadas e respostas à pandemia [online].** Rio de Janeiro: Observatório Covid 19; Editora FIOCRUZ, 2021, 221 p

CastroL. F. da S. O.; SilvaA. L. da; LimaM. A. de, et al. **Influenza e SARS-CoV-2: distinção clínica e imunopatológica no decorrer da pandemia da Covid-19.** Revista Eletrônica Acervo Saúde, v. 15, n. 3, p. e9963, 28 mar. 2022.

Franco C.G., Rodrigues E.C.A., Nascimento N.S, et al. **Infecção Por Coronavírus (Sars-Cov-2) Em Recém-Nascido Em Uma Maternidade Municipal Em Goiânia-Go.** The Brazilian Journal of Infectious Diseases. Volume 26, Supplement 1, January 2022, 102034

FILHO, A. D. S.F., **Indicação E Uso Da Azitromicina No Tratamento Da Covid-19: Uma Revisão Integrativa**. Mamografia apresentada ao Curso de Bacharelado de Farmácia da Faculdade de Enfermagem Nova Esperança do Mossoró (FACENE), 2021.

World Health Organization (WHO). **Frequently asked questions on Middle East respiratory syndrome coronavirus (MERS-CoV).** Disponível em: https://www.cdc.gov/coronavirus/mers/faq.html.

Yang X., Yu Y., Xu J., et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a singlecentered, retrospective, observational study. Lancet Respir Med., v. 8, n.4, e:26, 2020.

SOBREIRA, M.L.; MARQUES, M.A., **A panaceia dos anticoagulantes na infecção pela COVID-19.** J. vasc. bras. v.19, p. 1-2, 2020.

Zhai Z., Li C., Chen Y., et al. **Prevention and Treatment of Venous Thromboembolism Associated with Coronavirus Disease 2019 Infection: A Consensus Statement before Guidelines.** Thromb Haemost, v. 120, n. 06, p. 937-948, 2020.

RODRIGUES, B. A.; NUNES, C.P., Covid-19 E Tromboembolismo Pulmonar. Revista da Faculdade de Medicina de Teresópolis, v. 5, n. 1, 2022.

Hana H., Yanga L., Liu R., et al. **Prominent changes in blood coagulation of patients with SARS-CoV-2 infection;** Clin Chem Lab Med, v. 58, n. 7, p. 1116-1120, 2020.

Farhat F.G.L.C., Gregório H.C.T., Carvalho R.D.P., Avaliação da profilaxia da trombose venosa profunda em um hospital geral. J Vasc Bras., v. 17, n. 3, p. 184-192, 2018.

LOBASTOV, K., et al. **Prediction of Symptomatic Venous Thromboembolism in Covid-19 Patients: A Retrospective Comparison of Caprini, Padua, and IMPROVE-DD Scores.** Journal of Vascular Surgery: Venous and Lymphatic Disorders, v. 10, n. 2, p. 572-573, 2022.

Rodrigues, R.R., Correia, T., Guimarães H.P., et al. **Recomendações sobre Manejo da Anticoagulação nos Pacientes com COVID-19**. Associação Brasileira de Medicina de Emergência, 2020.

Gage B.F., Yan Y., Milligan P.E., et al. Clinical Classification Schemes for Predicting Hemorrhage: Results From the National Registry of Atrial Fibrillation (NRAF); Am Heart J. 2006 Mar;151(3):713-9. doi: 10.1016/j.ahj.2005.04.017.