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Case Report

Heart failure secondary to myocarditis after SARS-CoV-2 reinfection: a case report



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ABSTRACT

Introduction: Cardiac involvement in COVID-19 can range from mild damage to severe myocarditis. The precise mechanism by which COVID-19 causes myocardial injury is still unknown. Myocarditis following administration of COVID-19 vaccines, especially those based on mRNA, has also been described. However, no reports of heart failure following reinfection with SARS-CoV-2 in patients immunized with an inactivated vaccine have been identified.

Case description: The patient was a 47-year-old male construction worker of African descent, with type II diabetes and a history of infection by SARS-CoV-2 in December 2020 and May 2021, confirmed by RT-PCR. He received two doses of an inactivated vaccine against COVID-19. Between the two COVID-19 episodes with positive RT-PCR, he had two episodes of bacterial lung infection. After the second episode of SARS-CoV-2 infection, he was diagnosed with severe heart failure as a sequela of myocarditis.

Conclusion: It is essential to perform a thorough follow-up after infection with SARS-CoV-2 since, even with proper immunization, it is possible that the patient was reinfected and suffered severe cardiac sequelae as a consequence. The hypothesis of an etiology associated with the use of an inactivated vaccine against COVID-19, with a potential immune enhancement mechanism following reinfection with SARS-CoV-2, cannot be rejected.

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Introduction

Cardiac involvement in COVID-19 can range from mild damage to severe myocarditis. SARS-CoV-2 binds with high affinity to human angiotensin-converting enzyme receptor 2 (ACE 2), which is expressed in the entire body, including the heart. Severe systemic manifestations, such as myocarditis, have been reported in association with COVID-19 (Kerneis et al., 2021; Hamming et al., 2004). Some COVID-19 patients have persistent tachycardia, sustained asymptomatic hypotension, and bradycardia (Huang et al., 2020). Higher mortality has been demonstrated in patients with

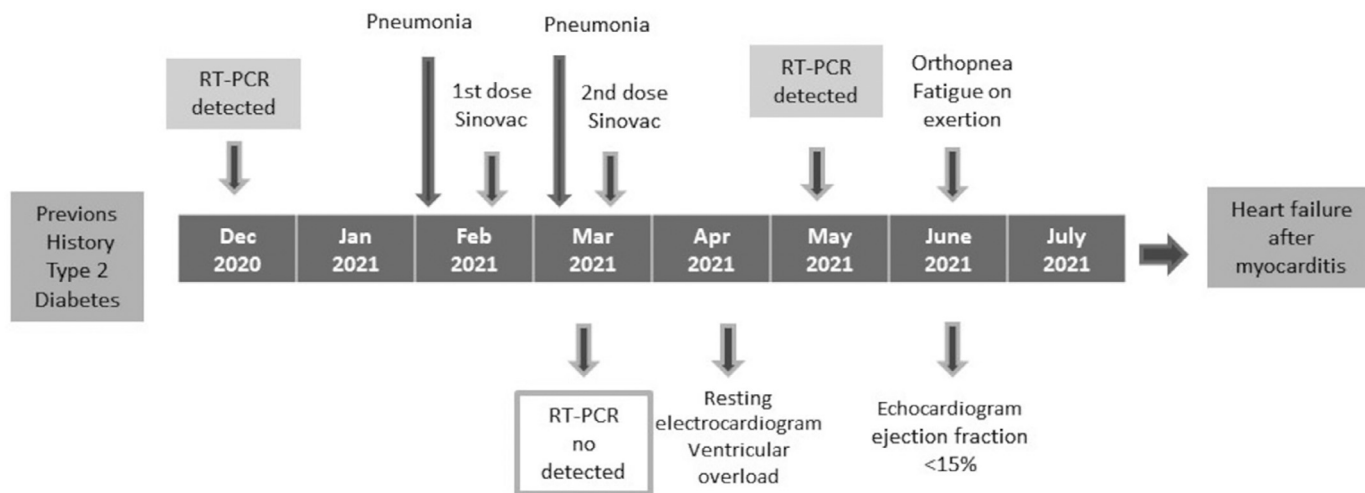


Figure 1. Case history timeline

COVID-19 – specifically, in patients who had acute myocarditis and acute myocardial infarction (AMI), as well as rapid-onset heart failure (Wang et al., 2020). The precise mechanism by which COVID-19 causes myocardial injury is still unknown. However, it is suspected that the main mechanisms involved in the myocardial lesions are direct damage to cardiomyocytes, caused by systemic inflammation, myocardial interstitial fibrosis, exaggerated cytokine responses by type-1 and type-2 T-helper cells, destabilization of coronary plaque, hypoxia, and interferon-mediated immune responses (Babapoor-Farrokhran et al., 2020).

There is concern about possible cases of myocarditis associated with vaccine administration. Myocarditis following administration of COVID-19 vaccines, especially those based on mRNA, has been described (CDC, 2021). However, no reports of heart failure following reinfection with COVID-19 in patients immunized with an inactivated vaccine have been identified. To date, the incidence of myocarditis and pericarditis, regardless of the type of vaccine applied, is low, having been reported in a previous study as 2–3 cases of myocarditis/pericarditis per million doses applied (Cai et al., 2021).

Case description

The patient was a 47-year-old male construction worker of African descent, with type II diabetes, who had a history of infection with SARS-CoV-2, with diagnosis confirmed by RT-PCR (reverse transcription polymerase chain reaction) on December 10, 2020, when he presented mild flu-like symptoms (cough, rhinitis, and myalgia). On February 10, 2021, he presented bronchopneumonia, identified by a chest X-ray, and was treated with the antibiotics azithromycin and amoxicillin with clavulanic acid; his symptoms improved, and RT-PCR was not performed. He received a first dose of the Sinovac immunizing agent – an inactivated vaccine against COVID-19 – on February 23, 2021.

On March 8, 2021, he presented a new condition of respiratory infection, with dyspnea and tiredness on moderate exertion. On March 9, 2021, he underwent an RT-PCR test for SARS-CoV-2, which was not detected. His cough and dyspnea persisted. On March 12, 2021, he underwent a chest X-ray that identified bilateral thickening of the fissures and mild bilateral opacities in the base of the lungs, leading to a diagnosis of pneumonia, which was treated with the antibiotic cefuroxime until March 20, 2021, when the patient showed clinical improvement and partial resolution of symptoms, with fatigue persisting on hard exertion. On March 23, 2021, he received a second dose of the immunizing agent Sinovac.

Resting electrocardiograms (ECGs) performed in January and April 2021 revealed sinus tachycardia and left ventricular overload, respectively. On May 3, 2021, the patient sought outpatient care due to a condition of productive cough, posterior chest pain, and sore throat associated with dyspnea on moderate exertion, initiating on May 1, 2021. His vital signs (temperature, blood pressure, and oxygen saturation) were stable, and he presented tachycardia (116 bpm). On May 3, 2021, an RT-PCR test for SARS-CoV-2 was positive, characterizing reinfection with COVID-19. The patient evolved with a mild condition, and returned to work on May 14, 2021, complaining of fatigue on hard exertion. In June 2, 2021, he presented tiredness and fatigue on minimal exertion, associated with feelings of suffocation and orthopnea that had started 2 days earlier; this required hospitalization. An echocardiogram identified diffuse hypokinesia, an ejection fraction of 15%, severe pulmonary arterial hypertension (PASP 71 mmHg), and non-sustained polymorphic ventricular tachycardia on exercising. During hospitalization, the patient presented 52 pg/mL troponin I, dilated and hypokinetic LV and RV in cardiac MRI, biatrial dilation, mitral and tricuspid insufficiency, and late enhancement of non-ischemic aspect, in addition to negative serology for Chagas disease, syphilis, and viral diseases. He evolved with clinical improvement, persisting with fatigue and dyspnea on moderate exertion, and is still being followed up in an outpatient clinic, with a diagnosis of heart failure probably secondary to myocarditis sequelae, following immunization with an inactivated SARS-CoV-2 virus vaccine, associated with a probable reinfection. Figure 1 depicts the case history timeline.

Discussion

Myocarditis is an inflammation of the myocardium, which can be caused by a variety of infectious (viruses, bacteria, and protozoa) and non-infectious diseases (Bozkurt et al., 2021). There are case reports of myocarditis and pericarditis following vaccination with mRNA COVID-19 immunizing agents, mostly in male adolescents, within a few days of vaccination against COVID-19 and, more often, after the second dose, as reported with our patient (CDC, 2021). Among the reported adverse effects experienced after SARS-CoV2 vaccination, the most frequent have been pain, fatigue, and headache, in addition to edema, fever, joint pain, and muscle pain (Cai et al., 2021). Other studies have demonstrated no serious adverse events reported within 28 days following administration of inactivated live virus vaccines (Xia et al., 2021; Saeed et al., 2021).

A previous diagnosis of COVID-19 may provide a degree of protection against new COVID-19 infection (Toniasso et al., 2021).

However, our patient, with a previous COVID-19 infection, who subsequently developed symptoms after a second dose of the SARS-CoV-2 vaccine, raises the possibility of a potential immune enhancement mechanism following previous immune exposure (Shaw et al., 2021). Moreover, this case, with myocarditis and severe heart failure, involving an inactivated SARS-CoV-2 vaccine associated with probable reinfection, reinforces the need for better knowledge of the natural history of COVID-19 and its sequelae (Boff et al., 2020). Studies have reported that almost all patients with vaccine-related myocarditis have demonstrated resolution of signs and symptoms, and showed improvement, with improved diagnostic and imaging markers with or without treatment (Singh et al., 2021). However, this was not observed in our patient, who continues to suffer from cardiac sequelae with severe heart failure.

Conclusion

Our case report reinforces the importance of an adequate interdisciplinary follow-up after SARS-CoV-2 infection, with greater surveillance and evaluation of adverse events after immunization. Even with adequate immunization, there is a possibility that the patient has been reinfected, presenting severe cardiac sequelae.

An etiological hypothesis for this case of myocarditis and heart failure may refer to the patient's previous history of diabetes mellitus (a risk factor for myocarditis), with his condition aggravated by the use of an inactivated vaccine against COVID-19 as a potential mechanism of immune reinforcement after recurrent infection with SARS-CoV-2.

Declaration of Competing Interest

The researchers declare that they have no conflicts of interest.

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Ethical approval statement

This study was approved by the Research Ethics Committee of Hospital de Clínicas de Porto Alegre.

References

- Babapoor-Farrokhran S, Gill D, Walker J, et al. Myocardial injury and COVID-19: possible mechanisms. *Life Sci* 2020;15(253).
- Boff da Costa R, de Castro Cardoso Toniasso S, Goldani L, Joveleviths D. COVID-19: concern about interrupting social isolation of healthcare workers and professionals. What should be done with the results of the available COVID-19 diagnostic tests? *Eur Rev Med Pharmacol Sci* 2020;24(23):12579–88. doi:10.26355/eurrev_202012_24055.
- Bozkurt B, Kamat I, Hotez PJ. Myocarditis with COVID-19 mRNA vaccines. *Circulation* 2021. doi:10.1161/CIRCULATIONAHA.121.056135.
- Cai C, Peng Y, Shen E, Huang Q, Chen Y, Liu P, Guo C, Feng Z, Gao L, Zhang X, Gao Y, Liu Y, Han Y, Zeng S, Shen H. A comprehensive analysis of the efficacy and safety of COVID-19 vaccines. *Mol Ther* 2021;29(9):2794–805. doi:10.1016/j.ymthe.2021.08.001.
- Centers for Disease Control and Prevention. Myocarditis and pericarditis following mRNA COVID-19 vaccination. 2021.
- Hamming I, Timens W, Bulthuis MLC, Lely AT, Navis GJ, van Goor H. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. *J Pathol* 2004;203(2):631–7.
- Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395(10223):497–506.
- Kerneis M, Bihan K, Salem JE. COVID-19 vaccines and myocarditis. *Arch Cardiovasc Dis* 2021;114(6–7):515–17. doi:10.1016/j.acvd.2021.06.001.
- Shaw KE, Cavalcante JL, Han BK, Gössl M. Possible association between COVID-19 vaccine and myocarditis: clinical and CMR findings. *JACC Cardiovasc Imaging* 2021 S1936-878X(21)00485-X. doi:10.1016/j.jcmg.2021.06.002.
- Singh B, Kaur P, Cedeno L, Brahimi T, Patel P, Virk H, Shamoan F, Bikkina M. COVID-19 mRNA vaccine and myocarditis. *Eur J Case Rep Intern Med* 2021;8(7). doi:10.12890/2021_002681.
- Saeed BQ, Al-Shahrabi R, Alhaj SS, Alkorkhardi ZM, Adrees AO. Side effects and perceptions following Sinopharm COVID-19 vaccination. *Int J Infect Dis* 2021;111:219–26. doi:10.1016/j.ijid.2021.08.013.
- Toniasso SCC, Fernandes FS, Joveleviths D, Filho FFD, Takahasi AY, Baldin CP, Pereira RM, da Silva LP, Brum MCB. Reduction in COVID-19 prevalence in health-care workers in a university hospital in southern Brazil after the start of vaccination. *Int J Infect Dis* 2021;109:283–5. doi:10.1016/j.ijid.2021.07.025.
- Xia S, Zhang Y, Wang Y, et al. Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBIBP-CorV: a randomised, double-blind, placebo-controlled, phase 1/2 trial. *Lancet Infect Dis* 2021;21(1):39–51. doi:10.1016/S1473-3099(20)30831-8.
- Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *Jama* 2020;323(11):1061–9.