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Case Report

Reactivation of COVID-19: A Case Report

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Abstract

COVID-19 has spread around the world, quickly becoming a pandemic. We present in this report a case of reactivation of COVID-19. The patient, an 84-year-old showed the typical respiratory symptoms, comorbidities such as hypertension, diabetes, grade V of kidney disease, and obesity. In addition, it is related to repetitive infections in the urinary tract. The data reported here contribute to a better understanding of SARS-CoV-2 reactivation cases.

Keywords: Novel Coronavirus Disease (2019-nCoV); SARS-CoV-2; Virus reactivation

Introduction

COVID-19 is a disease caused by a beta coronavirus family. SARS-CoV-2, a positive-sense, single-sense RNA virus, which taxonomically belongs to the family of viruses and *Sarbeco Fitenerus* that several other species cause human diseases graves [1].

Since its first appearance in China in December 2019, COVID-19 has spread rapidly worldwide, becoming a pandemic. Despite considerable efforts to contain the disease, the virus continued its prevalence in many countries with varying clinical manifestations. Health agents worldwide have expressed concern about a high rate of transmission of the virus, which has led to an overload of health services with the possibilities of reinfection and reactivation [2].

Virus reactivation occurs when in 30 days, the patient has a positive result for SARS-CoV-2, after at least two previous negative results. The possibility of reactivation of COVID-19 represents a significant public health problem since it can contribute to the increase in the transmission of the virus in the population [3].

Reactivation and reinfection are different clinical conditions of COVID-19. The WHO defines reinfection as the process by which a person was once infected with SARS-CoV-2, ceased to be infected, and became reinfected with SARS-CoV-2. However, in this case, a minimum period of 90 days is required for it to be considered reinfection [2]. In cases of reinfection or reactivation, the virus should be genetically sequenced in the first and second infection strains to see if they are viruses of the same lineage or different strains [4, 5].

The existence of cases of reactivation and reinfection should in no way change the public health and clinical management measures for cases of primary infection, nor the management of

secondary infections by COVID-19. It is important to emphasize that only with the existence of at least two samples, through which the primary infection and the secondary infection (primary sample and secondary sample) can be confirmed, reinfection and reactivation can be confirmed [3, 4].

Thus, it is relevant that cases of reactivation are reported, especially with morbidities, so that clinical evolution can be evaluated to enable a better scientific understanding of the viral transmission cycle and in the parameters associated with the patient.

Case report

We report an 84-year-old woman, who had multiple risk factors for progressing to a severe case; such as age, hypertension, diabetes, grade V chronic kidney disease and obesity, came to the emergency on 05/2020, lucid, oriented, and walking, with 96% O_2 saturation. She reported dysuria, cough, sore throat, low-grade fever (less than 38°C), dizziness, and chills for seven days. She also noted "feeling faint" on said date. She had recurrent urinary tract infections.

The management chosen was performing a chest CT. The CT study revealed faint ground-glass areas of peripheral and central distribution, predominantly in the upper lobe, and tomographic lung involvement of < 25% (Figure 1A)**.** Mechanical ventilation was necessary to stabilize the patient. The patient was discharged after 15 days of hospitalization. After 14 days the patient was admitted to the emergency room with behavior change, lowered level of consciousness, and dysuria. The patient was hospitalized for the treatment of a urinary infection and after 8 days the chest tomography showed bilateral ground glass pulmonary infiltrate, affecting more than 50% of the lung parenchyma (Figure 1B)**.** Real-time polymerase chain reaction (RT-PCR) SARS-CoV-2 identification result was positive. As with the first infection, mechanical ventilation was necessary. Lab tests was not performed in the first phase of infection, and in the second phase, IgG was negative and IgM positive. Only ten days after the second hospitalization, occur admission lab tests, whose result for IgG showed positive.

The patient had a positive urine culture for multidrug-resistant *Staphylococcus haemoliticus, Escherichia coli* + *Proteus*, and the fungus *Candida tropicalis.* The patient has showed a worsening of her respiratory condition, refractory hypotension and a new lowering of consciousness. Death occurred after 26 days of hospitalization. The PCR result was positive for COVID-19 throughout the second hospitalization.

During infection, the first RT-PCR sample on 10/05/2020 presented a value of Ct 17 and in an examination performed on 07/01/2020, the day before the patient died, the Ct was 22. The two values presented induce an infection at the height of its course.

A genotyping test was performed on samples from the two episodes of the disease in the patient. Both samples showed the same results for the deletion of SARS-CoV-2, suggesting that they are the same variant, which can be B1.1.28, B1.1.33, P2 or Delta according to the Fiocruz Genotyping Kit.

The patient was treated in the first infection with antibiotic Levofloxacin, anticoagulant treatment with Enoxaparin, anti-inflammatory Dipyrone, and opioid Tramadol. In the second hospitalization, the patient was treated with steroids, and antibiotics, Levofloxacin, Ertapenem, Meronepenem, Daptomocin, Polymyxin B, Amikacin, and Anidulafungin.

Regarding clinical data, in the first infection, there was a drop in lymphocyte values with the value of 520/mm^3. The D-dimer values reached 1950 ng/mL in the first infection and 1700 ng/mL in the second sample. On 06/30/2020, the patient had a maximum value of 3110 ng/mL. There were no changes in ALT and AST enzymes, and in the C-reactive protein (CRP) technique, no changes were observed in the first and second infections.

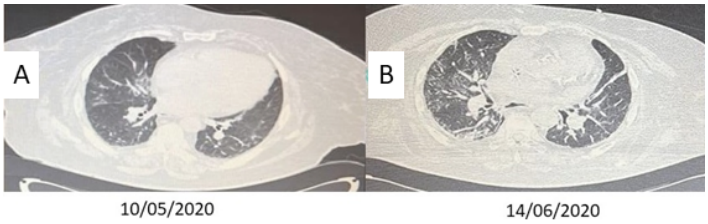

Figure 1A: First admission. Tenuous ground-glass areas of peripheral and central distribution, predominantly in the upper lobe, and tomographic lung involvement below 25%. **1B: Second admission**. Bilateral ground-glass pulmonary infiltrate involves more than 50% of the lung parenchyma

Discussion

COVID-19 reactivation represents a major health concern, as it could significantly contribute to the spread of the virus in the population[1]. This relevance remains even with the changing panorama of the pandemic in Brazil.

In 2020, a systematic review and meta-analysis where fourteen studies of 2,568 subjects were included showed that the incidence of recurrent positivity for SARS-CoV-2 was 14.8%. The combined estimate of the interval from disease onset to recurrence was 35.4 days and from the last negative to recurrent positive result was 9.8 days. In this study, the estimate the disease beginning to the recurrence was 27 days, and the interval between discharge and return to the hospital was 12 days.

Azam *et al.* (2020) reported younger patients with the more prolonged initial disease presented recurrent positivity for SARS-

CoV-2, while patients with diabetes and low lymphocyte counts were less likely to have cases of reactivation[6]. The patient had diabetes, hypertension and chronic kidney disease, which puts her in the risk groups of those infected by COVID-19. In addition, she had recurrent Urinary Tract Infection (UTI) and at the time of admission, the patient had a UTI. Risk factors for reactivation include host status, virological characteristics, and steroid-induced immunosuppression[1].

The selected patient met the reactivation criteria, having diabetes, hypertension, and chronic kidney disease, which places her in the risk group of those infected by COVID-19. It is important to note that the urothelium of the bladder, and the kidney, harbors cells that express ACE2, the receptor for the spike protein of SARS-CoV-2 [7]., which may contribute to yet another case of urinary tract infection in the patient or even worsen as happened in the second hospitalization. 50% of patients who died from COVID-19 are reported to have secondary bacterial infections, which further intensifies the physiological progression of COVID-19 [8].

Detection in infected patients often fluctuates due to the occurrence of negative results in the molecular test, which may be due to the operator's experience in sample collection, sampling site, and viral load [9].

Alonso *et al*., 20219 reported a case of reactivation in Brazil where the patient showed symptoms of COVID-19 on 04/26/2020, and on 05/05/2020, the antibodies were negative. In June, the disease recurrence was on the 6th, and the antibodies were also negative when testing on the 8th. We only observed positive IgM and IgG antibodies on the 22nd of that month.

Ravioli, Ochsner & Lindner, described two cases of reactivation. In one of them, the patient had non-severe symptoms and was discharged and after returning to the hospital with symptoms, she died as well as the patient in our study. However, in the case mentioned in the publication, there were no reports of another active infection [11].

Although our patient's return was due to a new urinary infection, the chest CT indicated worsening of COVID-19 in the patient. In the first hospitalization, the involvement was 25% and in the second hospitalization, the involvement reached more than 50% of the pulmonary parenchyma.

In the scenario of the SARS-CoV-2 pandemic, patients with COVID-19 and microbial co-infection are characterized by lymphopenia and increased levels of pro-inflammatory cytokines in plasma [8], as well as the case described in this report.

Although the patient's urinary infection was present before SARS-CoV-2 infection, lymphopenia was observed in the patient during her first hospitalization.

The significant lymphopenia presented by the patient at the first infection reached the value of 10% of the total count, which is half of the minimum reference value which is 20%. This data is in accordance with the work of Cui et al. (2020) who reported the decrease in lymphocytes as a common factor in patients with COVID-19 [11].

It is assumed that elderly patients and those with more underlying diseases are more likely to develop immune dysfunction and have a higher risk of venous thromboembolism due to low immunity [12]. This dysregulation affects lymphocytes, and T cells are more susceptible to SARS-CoV-2, as the count of these cells can reach almost half of the lower reference limit. Patients with severe novel coronavirus pneumonia are more likely to be harmed [13]. Furthermore, the expression of T cells associated with messenger RNA can lead to venous thromboembolism [14]. The values had already increased in the patient's second infection, approaching the minimum reference value.

D-dimer levels from a value greater than 1,500 ng/mL have a sensitivity of 85% and specificity of 88.5% for detecting events suggestive of deep vein thrombosis [15, 16]. NEMEC The patient had values higher than those reported for both infections (1950 and 1700 ng/mL, respectively).

In COVID-19, cardiovascular changes and abnormalities in clotting parameters are described. The reasons for these changes are not fully understood, but studies show a correlation between elevated clotting markers and increased fatality rates among people with COVID-19 [12].

The relationship between changes in the coagulation mechanisms of patients with COVID-19 and the increase in lethality rates point to the occurrence of thrombotic events such as disseminated intravascular coagulation (DIC), deep vein thrombosis (DVT), and pulmonary embolism (PE) [15-18].

The literature shows a limited number of reports on reactivation. However, it is essential to report and conduct analyses to discover the reasons for such an event. The WHO has not officially decreed the end of the pandemic. And yet, for some time, studies must be carried out on COVID-19 to understand and prepare for other possible viral threats, as well as more efficient vaccines and more effective drugs.

In the case reported, the patient died after the reactivation of COVID-19, probably due to the presentation of a more critical spectrum of the disease associated with age and the comorbidities presented.

The data in this report may contribute to a better understanding of the reactivation cases caused by SARS-CoV-2. It is essential to carry out more detailed studies so that the cases are increasingly elucidated.

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