Covid-19 and HIV: Not Always an Unfavorable Combination

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Case report

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Abstract

Background

A 73-years-old-man patient who had a history of Human Immunodefiency Virus (HIV) infection for over 20 years was diagnosed with SARS-CoV-2 infection.

Case presentation

The patient was admitted to the Intensive Care Unit (ICU), where he remained for 25 days, due to a severe condition. Intubation, hemodialysis and tracheostomy were necessary to maintain homeostasis. In addition to regular treatment with etravirine, dolutegravir, darunavir and ritonavir for highly active antiretroviral therapy, the patient received To-cilizumab, which showed a great recovery in the patient's condition.

Conclusion

The patient had several risk factors, such as: male gender, age> 70 years and hypertension. The use of To-cilizumab was of great importance in the patient's recovery, since the drug increased his immune response, which is deficient, due to HIV infection.

Background

A 73-year-old patient with a history of Human Immunodeficiency Virus (HIV) infection for more than 20 years was diagnosed with SARS-CoV-2 infection. The patient was admitted to the ICU, where he remained for 25 days. In addition to regular treatment, the patient received To-cilizumab, showing excellent recovery from severe symptoms.

Thus, we aim to show how important the implementation of the immunosuppressant was to help in the immune response against COVID-19, together with the non-interruption of the highly active antiretroviral therapy.

Introduction

Since December 2019, an outbreak of COVID-19 appeared in Wuhan, China. The etiological agent was identified as a novel coronavirus closely related to the former epidemic SARS-CoV, therefore named SARS-CoV-2, a medium-sized enveloped RNA virus. The disease, COVID-19, was recognized as a pandemic by World Health Organization (WHO) on March, 2020. As the date publication of this report, more than 1,000,000 deaths due COVID-19 were confirmed (1).

COVID-19 presents as a risk for people living with HIV (PLHIV), particularly in those with low TCD4+ cell count, high viral load and other comorbidities. The infection rates in PLHIV carriers are still uncertain, once there are few published literatures relating COVID-19 co-infection in PLHIV (2).

In the present report, we describe a case of a 73-year-old-man HIV-positive that progressed to Severe Acute Respiratory Syndrome (SARS) with a successful outcome.

Case Report

On March 21, a 73-year-old man, entered the emergency room complaining of fever and dyspnea progressing over 10 days. Physical examination showed axillary temperature = 38.6ºC, blood pressure BP = 103/73 mmHg, heart rate = 88 bpm, respiratory rate = 39 bpm and pulse oximetry = 89% (O_2 nasal cannula with 3 L/min). He was put under non-rebreather mask with 10 L/min and was admitted to the ICU.

He had history of HIV infection for over 20 years, regularly treating with etravirine, dolutegravir, darunavir and ritonavir for highly active antiretroviral therapy (HAART). The last TCD4+ cell count was above 500/ µL and the viral load was undetectable for more than 5 years. He also had previous diagnosis of systemic arterial hypertension (SAH) and no history of diabetes mellitus or smoking.

On the day of admission, a nasopharyngeal swab was collected, and the RT-PCR for SARS-CoV-2 resulted positive. The virus panel for others agents was negative.

A chest *computed tomography* (CT) scan on admision (**Figure 1-A**) showed multiple ground-glass opacities, affecting all pulmonary lobes with predominantly peripheral distribution, associated with consolidation on lower lobes, with accented pulmonary involvement (> 50%). Empirical broad-spectrum antimicrobial therapy with ceftriaxone and azithromycin was started, the HAART was maintained and enoxaparin was prescribed (40mg/day).

The laboratorial exams revealed high percentage of white blood cell, a normal neutrophil count 6,410/mm^3 (normal range: 1,700-7,000/mm^3), a normal percentage lymphocyte count 1,050/mm^3 (normal range: 900-2,900/mm^3). There were elevated blood levels of C-reactive protein (PCR) 34,17 mg/dL (normal range: 0-5 mg/dL), D-dimer 8,469 ng/mL (normal range: < 0.5 ng/mL), and Lactic Dehydrogenase (LDH) 592 U/L (normal range: 240-480 U/L). The viral load was undetectable, and the CD4 cell count was 876 cell/mm^3 (normal range: 404-1,612 cell/mm^3), CD8 cell count was 876 cell/mm^3 (normal range: 229-1,129 cell/mm^3).

On March 22, endotracheal intubation was performed and the patient underwent mechanical ventilation with FIO2 60%, PEEP 8 mmHg and pressure support 20 mmHg. Blood gas analysis revealed pH 7.32 (normal range: 7.35-7.45), pO2 116 mmHg (normal range: 30-50 mmHg), pCO2 38 mmHg (normal range: 35-45 mmHg) and SatO2 98% (normal range: 94-100%). Hydroxychloroquine (HCQ), Azithromycin and Ceftriaxone were prescribed besides previous use of Etravirine, Dolutegravir, Darunavir and Ritonavir for HIV as maintenance treatment. On March 27, the use of Azithromycin and HCQ was interrupted and a Sulfamethoxazole-Trimetroprim in a prophylactic dose (800/160 mg/day) was initiated, due to TCD4+ cells count = 92 µ/L.

On March 29, cultures identified *Staphylococcus epidermidis* (central venous catheter blood), *Staphylococcus hominis* (central venous catheter blood) *and Candida dubliniensis* in the tracheal secretion and Meropenem, Linezolid and Micafungin were incorporated to the treatment. HIV viral load remained undetectable during this period.

On March 29th, the creatinine level was 2.4 mg/dL (normal range: 0.7-1.3 mg/dL) and he presented low diuresis (700 mL/24 hours), revealing a worsening in kidney function, and continuos veno-venous hemodialysis (CVVHD) was initiated. On early April, the interleukin-6 (IL6) measurement was 79.3 pg/mL (reference value: 1.5 – 7 pg/mL). On April 3rd, the patient received to-cilizumab 8 mg/kg (600 mg) intravenously. One day after, was patient's first day without fever since admission, and started to improve progressively.

On April 7th, tracheostomy was performed, and five days later, he presented an improvement on respiratory condition - CT done on April 15th showed a significant improvement on pulmonary involvement (**Figure 1-B**) and mechanical ventilation was no longer needed.

On April 15th, the patient was discharged from the ICU and seven days later the tracheostomy was removed. On May 1st the patient was discharged from the hospital, and no prescription was needed unless the use of his regular medications. Clinical chronologic outcome is showed on **Figure 2**.

Discussion

Worldwide, there are approximately 37.9 million PLHIV and under a higher risk of being exposed to SARS-CoV-2 (2). In Brazil, 966,058 people have been infected since 1980, being 51.2% in the Southeastern area, where the city of São Paulo is located (3). According to Centers for Disease Control and Prevention (CDC), people with HIV are in the COVID-19´s risk group, needing extra precautions. It also affirms that people with low CD4 cell count and those who are not on HIV treatment (HAART) are under an even higher probability of getting sick (4).

HIV physiopathology consists of destroy the immune cells system and specific antibody responses, which in cases of COVID-19 association may cause a longer course of the disease (5). A recent study has shown that acute respiratory infections increased mortality in HIV-positive people in Africa (1). Nevertheless, studies from other countries presented a different outcome, showing that COVID-19 and PLHIV association didn't impact the survival. (6)

The fact that the patient was already taking antiretroviral medication is a hypothesis that would explain this scenario (6). Another factor that seems to have a positive impact on the outcome of the patients is the undetectable viral load, as recent studies suggests it results in a better general prognosis (2).

Generalized immune activation and systemic CD4 lymphocyte depletion occurs in the chronic phase of untreated HIV, also, the remaining T cells may initiate abnormal responses to antigens. The lymphocyte B dysfunction results in abnormal polyclonal activation and lack of specific antibody responses. COVID-19

causes a significantly reduce in the total number of lymphocyte B, lymphocyte T and natural killer (NK) cells. The pathophysiology of the severe cases is not yet fully understood, but it appears not only to be related to virulence factors of the pathogen, but also to the dysfunctional and self-aggressive immune response triggered by the infection. This phenomenon has been called “cytokine storm” and usually occurs in the second week of infection for COVID-19, which was observed in the patient in this brief report, admitted on the tenth day of symptoms[8].

A recent study suggests that SARS-CoV-2 may damage lymphocytes, especially T lymphocytes, and the immune system was harm during the period of disease (5). In addition to these findings, a characteristic of COVID-19 patients is an increased laboratorial level of PCR, D-dimer and LDH, as our patient presented on the admission exams, the lung is the main organ affected by this virus, which will cause microvascular lesions, due to a systemic inflammatory response (SIR). The intestines and kidneys also have receptors that are affected by SIR, but the main concern are the kidneys, which by this process can generate low diuresis, proteinuria and changes in the amounts of albumin in the urine, requiring hemodialysis. (6,7)

HIV infections can be classified in five stages (0,1,2,3, or unknown), depending on negative/indeterminate result (stage 0) or test results of CD4+ T-lymphocyte associated or not with opportunistic illness. Our patient presented CD4+ lymphocyte count 876 Cells / µL, being classified as stage 2 (750–1,499 Cells / µL) according to CDC classification (8). The undetectable viral load was probably a crucial factor for the patient’s positive disclosure, besides previous use of Darunavir (HAART).

Our patient is over 60-years-old-man, presenting immunodeficiency, characterized by decreased in immunological system functions. These alterations trigger a rise in the incidence and severity in infectious diseases, explaining the risk of COVID-19 in this group (9). Besides being elderly, the patient has a history of SAH. When this chronic disease is treated with ACE inhibitors, present upregulation of ACE2 receptor and the raise expression of ACE2, could facilitate the viral entry (10). Beyond that, heart and lung present a high expression of ACE2 receptors (11).

Regarding treatment, the use of tocilizumab, HAART and broad-spectrum antibiotics is in accordance with the most recent literature for the treatment of COVID-19 in patients with impaired immune system functions. The only medication that has not been administered is dexamethasone, which has an important reducing factor in lung injuries and has been shown to reduce mortality in patients hospitalized with SARS-CoV-2. (12)

Conclusion

The reported patient presents the following variables as risk factors: male sex, age > 70 years and hypertension. Despite HIV infection, the patient had good adherence to HAART, TCD4 cells > 500 / µL and long-standing undetectable viral load. We choosed to maintain HAART throughout the hospitalization and

this decision may have contributed to the good outcome. It is possible that all the severity of the case was due to infection by SARS-CoV-2 and dysfunctional immune response.

Abbreviations

Human Immunodefiency Virus – HIV

Intensive Care Unit – ICU

People living with HIV – PLHIV

Severe Acute Respiratory Syndrome – SARS

Highly active antiretroviral therapy – HAART

Systemic arterial hypertension – SAH

Computed tomography – CT

C-reactive protein – PCR

Lactic Dehydrogenase – *LDH*

Hydroxychloroquine – HCQ

Continuos veno-venous hemodialysis – CVVHD

Centers for Disease Control and Prevention – CDC

Natural killer – NK

Systemic inflammatory response – SIR

Declarations

Ethics approval : We declare that this case report was approved by the ethics committee of Hospital Alemão Oswaldo Cruz.

Consent for publication : Not applicable.

Availability of data and materials: All data generated or analysed during this study are included in this published article [and its supplementary information files].

Competing interests: The authors declare that they have no competing interests.

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Figures

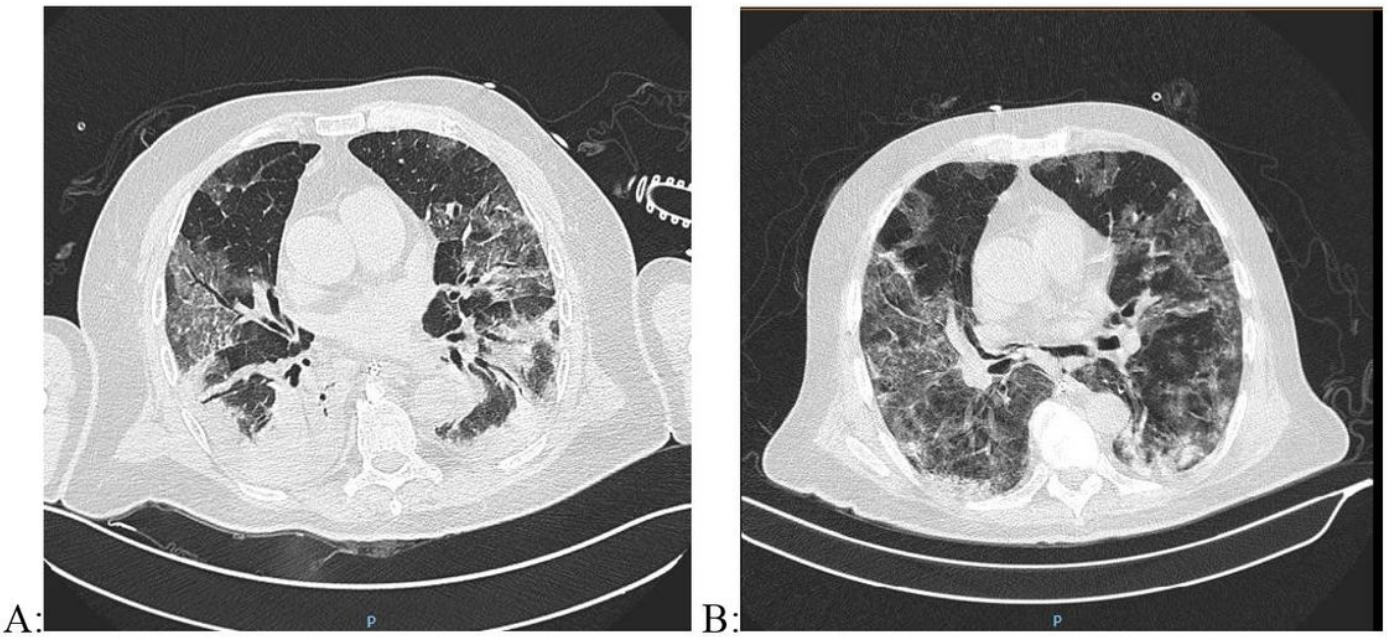

Figure 1

A: CT showing ground glass opacity (GGO) areas with the presence of consolidation areas in the posterior region. B: CT with replacement of the consolidation for ground glass opacity (GGO) areas, demonstrating significant improvement of the clinical condition. A: CT on the admission day; B: CT after 22 days of hospitalization.

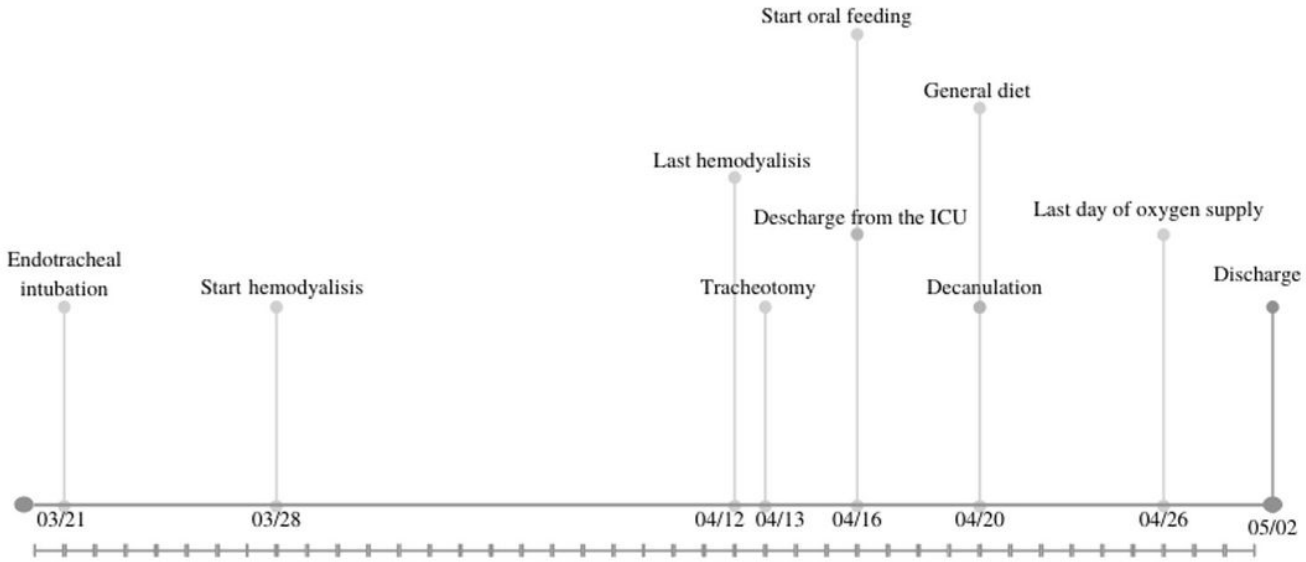

Figure 2

Patient’s clinical evolution and procedures over time.