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Case Report

Sequential dosing of convalescent COVID-19 plasma with significant temporal clinical improvements in a persistently SARS-COV-2 positive patient

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ABSTRACT

The current global pandemic, SARS-CoV-2 infection, is still extending across the world affecting millions of lives to the date. While new successful vaccines are available with promising outcomes to minimize the spread and to reduce the severity of the disease, optimal therapeutic options still remain elusive. COVID-19 convalescent plasma (CCP) is an investigational treatment option which studies suggesting signals of efficacy and favorable outcomes only for patients treated very early in course of the disease. Benefits of the use of CCP later in the disease remain highly debated and therefore are not common practice. We hereby report a case of severe SARS-CoV-2 infection in a young male patient with prolonged COVID-19 positivity who received repeat doses of CCP treatments later in the disease with temporal clinical improvement. This patient's case highlights the need of further studies evaluating efficacy of repeated dosing of CCP. This also suggests a potential of successful use of CCP later in the disease in selected COVID-19 patients.

1. Introduction

The current global pandemic, SARS-CoV-2 infection, is still extending across the world affecting millions of lives to the date. While new successful vaccines are available with promising outcomes to minimize the spread and to reduce the severity of the disease optimal therapeutic option still remain elusive. COVID-19 convalescent plasma (CCP) is an investigational treatment option which some trials suggesting signals of efficacy and favorable outcomes for patients very early in course of the disease. Benefit of the use of CCP later in the disease is not yet determined and therefore not in common practice. We hereby report a case of severe SARS-CoV-2 infection in a young male patient with prolonged COVID-19 positivity who received repeat doses of CCP treatments later in the disease with temporal clinical improvement.

2. Case summary

A 49-year-old overweight male (BMI = 26.6) with hypertension, uncontrolled type-2-diabetes mellitus, chronic obstructive pulmonary disease was admitted with 1-week history of dyspnea, productive cough, and fever. The patient tested positive for SARS-CoV-2 by PCR on day of admission. Upon admission, the patient was febrile, tachycardic, normotensive, and saturating 98–99 % on room air. Physical exam revealed clear lungs. Chest X-ray (CXR) at admission revealed ill-defined bilateral ground glass and reticular opacities (Fig. 1A). Patient's oxygen requirement increased during the hospitalization, necessitating intubation and mechanical ventilation on day four of the admission (Fig. 1B). His PaO2/FiO2 ratio was 232 mmHg indicating mild acute respiratory distress syndrome (ARDS). Two days following intubation, due to the patient's worsening clinical condition and radiological presentation

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(Fig. 1C), the patient was transfused with one unit (314 mL) of COVID-19 convalescent plasma (CCP). The patient's radiographic improved significantly within 48 h of the CCP transfusion (Fig. 1D). On the day of transfusion, his PaO2/FiO2 ratio was 290 mmHg; this gradually improved to 305 mmHg 5 days after transfusion. With convalescent plasma therapy, the patient showed improvement of inflammatory markers including LDH, CRP and Ferritin (Fig. 2). The patient was gradually weaned off of mechanical ventilation, and extubated 7 days after first CCP administration.

However, 2 days following extubation, the patient again exhibited respiratory distress and hypoxia with development of new CXR infiltrates, necessitating re-intubation. The patient again met eligibility criteria for CCP and a second unit of CCP was transfused (357 mL). Of note, the patient was still SARS-CoV-2 RNA positive at the time of second transfusion. There was temporal improvement in patient's clinical status and inflammatory markers after the second CCP transfusion (Fig. 2). The patient was extubated seven days after the second unit of CCP and discharged home on room air. There were no reported reactions to CCP during both the transfusions.

On retrospective analysis, robust signal-to-cutoff (S:Co) and IgG ratios at (>8), for Abbott and Euroimmun assays respectively, were seen for both the CCP units (preliminary data suggests ratios >4 correlate with a neutralizing antibody titer >1:200) [2]. Of note, patient was not tested for SARS-CoV-2 antibodies prior to either CCP doses.

The patient did not receive remdesivir or dexamethasone during hospitalization. Hydroxychloroquine was ordered on admission but was discontinued after 1 dose due to QTc prolongation. The patient also received azithromycin and vancomycin from days 1−5. He was also treated with IV furosemide which was later changed to IV bumetanide drip. IV cefepime, linezolid, and metronidazole were started on day 16 (during second intubation) as empiric coverage for possible aspiration pneumonia; these were continued until complete recovery was attained.

3. Discussion

This unique case highlights the temporally associated clinical and laboratory improvements following sequential dosing of CCP in a persistently SARS-CoV-2 RNA positive patient. While definitive cause and effect cannot be confirmed, this report provides signals of efficacy with repeated dosing of CCP in a younger patient, much later in the course of disease.

Patients diagnosed with ARDS secondary to SARS-CoV-2 may have positive PCR test results for multiple weeks after the onset of symptoms. Therefore, the clinical relevance of patient's 2nd positive PCR result is not clear [1]. Of note, the PCR CT values or viral load titers were not tracked for the patient. This information could possibly have contributed to the second dose CCP decision as well as timing.

Evolving evidence supports efficacy of early transfusion of CCP to prevent severe SARS-CoV-2 infection in patients [3] and further supports the use of high titer CCP for better clinical outcomes [4]. Early CCP dosing has become the practice in treating patients admitted with SARS-CoV-2 infection currently in the hospital settings. However, there is not enough evidence available advocating the use of CCP later in the course of the disease or its benefits in persistently SARS-CoV-2 RNA

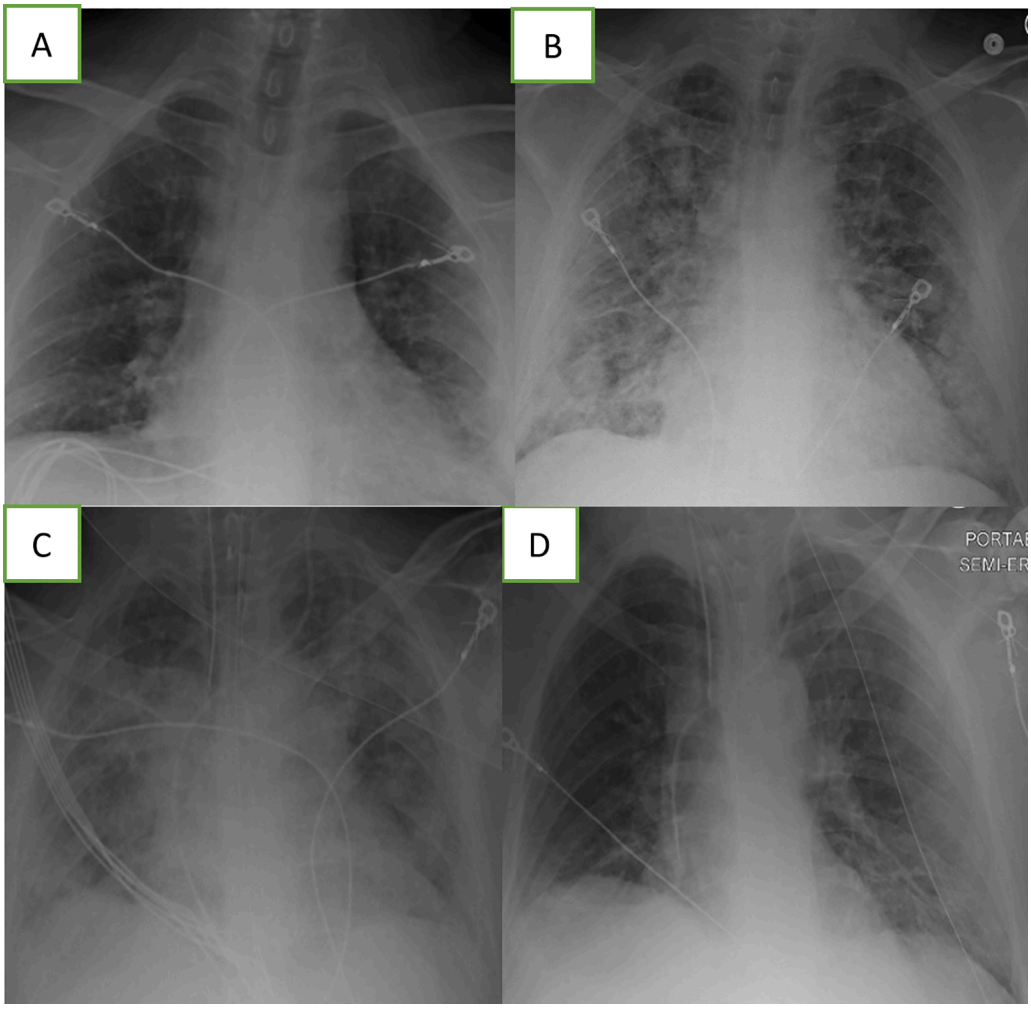

Fig. 1. Chest x-rays before and after CCP treatment.
(A) Chest X-ray upon admission revealing minimal ill-defined bilateral ground glass and reticular opacities.
(B) Chest X-ray prior to intubation revealing extensive bilateral consolidation and ground glass opacities.
(C) Chest X-ray, 18 h post intubation before convalescent plasma revealing extensive bilateral consolidation and ground glass opacities.
(D) Chest X-ray, 32 h after receiving convalescent plasma therapy revealing significant interval improvement in bilateral opacities.

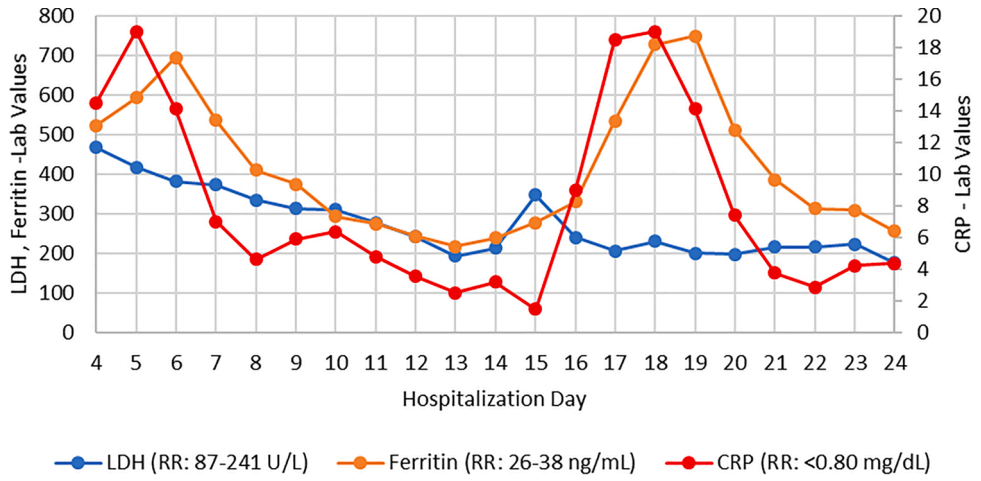

Fig. 2. Graph representing temporal decrement of inflammatory markers after receiving convalescent plasma therapy.

positive symptomatic patients [5]. Furthermore, the benefits of multiple dosing of CCP during the illness is yet to be determined. Therefore, this case underscores the need to investigate multiple dosing of CCP, in SARS-CoV-2 RNA positive symptomatic patients especially later in the disease [6].

Consent

Informed written consent was obtained from the patient for publication of the case report and the images.

CRediT authorship contribution statement

Our case has not been previously published and is not under consideration in any other peer-reviewed media. **Noupama Mirihagalle**, **Priyanka Parajuli**, **Vidya Sundareshan**, **Debadoot Saha**, **Arpan Shah**, **Francine Chua**, **Sana Waqar**, **Vidhya Prakash**, **Aaron A. R. Tobian**, **Evan M. Bloch**, **Louis Katz** and **Ruchika Goel** have read and approved the manuscript.

Declaration of Competing Interest

No relevant conflict of interest, financial or other, exists.

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