**Prolonged COVID-19 Disease in a Patient with Rheumatoid Arthritis on Rituximab Therapy**

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**Footnote Page**

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**Key Words:** Prolonged COVID-19, SARS-CoV-2, COVID-19, Rituximab, Convalescent Plasma, Immunosuppression, B-Cell Depletion, Remdesivir

**Abbreviations:**

ASH - The American Society of Hematology

COVID-19 - Coronavirus Disease 2019

CT - Computed Tomography

EUA – Emergency Use Authorization

NP-RT-PCR – Nasopharyngeal Reverse Transcription Polymerase Chain Reaction

RA - Rheumatoid Arthritis

RT-PCR – Reverse Transcription Polymerase Chain Reaction

SARS-CoV-2 - Severe Acute Respiratory Syndrome Coronavirus 2

**Introduction:**

We read with interest a brief report by Helleberg et al which describes the fascinating case of a Caucasian male in his fifties who had received treatment with rituximab and developed a prolonged coronavirus disease 2019 (COVID-19) infection [1]. Treatment with 2 courses of remdesivir temporarily abrogated his symptoms; however, after convalescent plasma (CP) treatment on day 58, his symptoms abated 2 days later, and he was discharged with disease resolution. This brief report and the concept of combined antiviral and antibody treatment has influenced our management for patients who are B-cell depleted with COVID-19.

Here we report a 50-year-old female being treated with rituximab for rheumatoid arthritis (RA) who also developed a prolonged course of COVID-19. She responded well to a treatment regimen of remdesivir and CP. We review the current literature for CP use in COVID-19 and argue for its use in B-cell depleted patients with prolonged symptoms.

**Case Presentation:**

A 50-year-old female with RA presented in July 2020 with persistent fevers and malaise for 4 months. She had been receiving rituximab injections regularly. In March, she developed fever, anosmia, ageusia, fatigue, decreased appetite, diarrhea and myalgias. In April, she tested positive for COVID-19 on nasopharyngeal reverse transcription polymerase chain reaction (NP-RT-PCR). She presented twice to the emergency department in April, was not hypoxemic, and was discharged.

In May, she was admitted for persistent fevers and dyspnea. Computed Tomography (CT) chest demonstrated patchy lower lobe opacities (Figure 1). She improved initially after

receiving antibiotics and was discharged home; however, she required readmission in June for persistent fever and malaise. CT chest showed new areas of ground glass opacities. An extensive workup for fever of unknown origin was unrevealing (see Supplementary Table 1). Laboratory analysis demonstrated hypogammaglobulinemia, and absent CD-19 cells. She was treated with intravenous immunoglobulin and oral methylprednisolone and discharged after fever resolution.

Two-weeks later, her symptoms returned, and she was readmitted for further evaluation. NP-RT-PCR and serum antibodies were negative for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and inflammatory markers were elevated (see Supplementary Table 2 and 3). Chest CT demonstrated increasing ground glass opacities and new consolidations. A bronchoalveolar lavage RT-PCR was positive for SARS-CoV-2. Bronchial cultures were negative for bacterial, acid-fast, and fungal infection. She was started on a 5-day course of remdesivir and received 2 doses of CP infusions. Her original complaints resolved after 48 hours and she returned home. 2-months later CT chest demonstrated complete radiographic resolution of abnormalities. She remains asymptomatic 8 months after discharge.

**Discussion:**

The use of CP to treat patients with SARS-CoV-2 has remained inconsistent and guidance in the immunocompromised is scarce. A recent trial compared 228 people who received CP to 105 who received placebo, revealing no differences in clinical status or mortality [2]. Only 6 patients in the treatment group (2.6%) and 3 in the placebo group (2.9%) were prescribed immunosuppressants. Another trial testing CP with high IgG titers in older adult patients within 72-hours after the onset of mild COVID-19 symptoms showed

decreased disease progression [3]. Patients with immunosuppressant use were excluded from randomization.

Immunocompromised patients can have a prolonged disease course when infected with SARS-CoV-2. Successful and safe treatment strategies are crucial to guide clinicians as it is unlikely that there will be large, randomized control trials examining optimal therapeutic strategies for patients with a lack of humoral protection. The American Society of Hematology (ASH) recently published a proof-of-concept study in which 17 B-cell depleted patients with prolonged COVID-19 were treated with CP. All but 1 patient had symptom improvement within 48 hours [4], consistent with the findings from Helleberg et al., and our experience.

As of March 9, 2021, the Food and Drug Administration reissued authorization for continued use of CP under Emergency Use Authorization (EUA), allowing use of high titer COVID-19 CP for hospitalized patients early in the disease course, or for those who are hospitalized with impaired humoral immunity [5]. This EUA permits CP use outside of the IDSA guidelines [6], allowing for the innovative and successful treatment seen in the original brief report by Helleberg et al., our patient, and the case series published by ASH. Future clarification of CP guidelines is needed regarding the use of combined remdesivir and CP in patients with B-cell depletion who have prolonged symptoms.

**References:**

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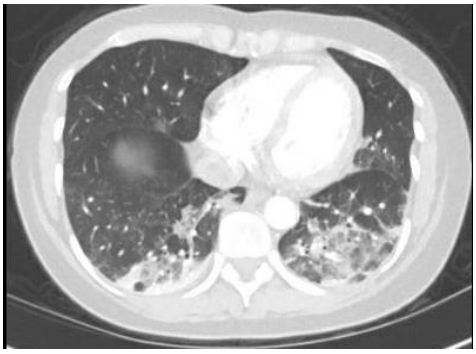
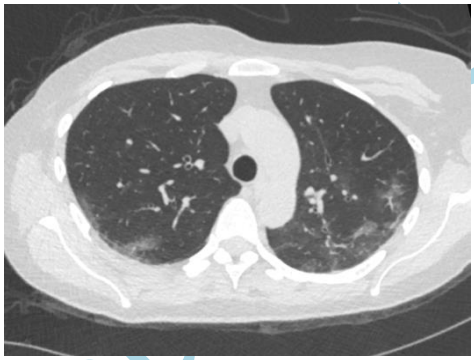
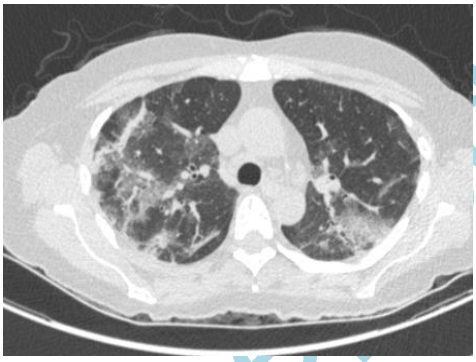
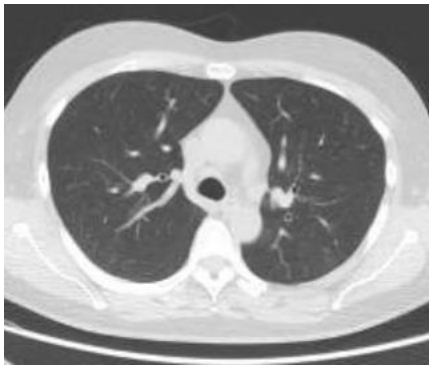
**Figure 1: Progression of CT scan findings**

Interval CT scans showing evolving and resolved ground glass opacities and consolidations.

CT = computed tomography.

**Figure 1: Progression of CT scan findings**

| CT Chest 5/9/2020 | CT Chest 6/25/2020 |
|---|---|
|  |  |
| **CT Chest 7/23/2020** | **CT Chest 9/28/2020** |
|  |  |