# Persistent COVID-19 Pneumonia in a Patient on Long-term Rituximab Therapy

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## Background

The viral dynamics and clinical course of SARS-CoV-2 infection in patients treated with immunomodulatory therapies remain unclear[1]. Here we describe an unusual case of persistent COVID-19 pneumonia in a patient who had received prolonged rituximab therapy for B-Cell lymphoma.

## Methods

The medical record relating to the patient's hospital admission was reviewed. This was followed by a systematic literature review of COVID-19 in the context of rituximab therapy.

## Case

A 59-year-old woman presented in February 2021 with a 2-week history of fevers. She had been diagnosed with COVID-19 a month previously (day 0) and had experienced mild upper respiratory tract symptoms for 1 week. Her medical history was significant for low grade B-cell lymphoma diagnosed in 2016 for which she received 2 monthly rituximab infusions for the past 2 years. The last dose of rituximab was given 2 months prior to acquisition of SARS-CoV-2.

On admission to hospital (day 30) she had a positive nasopharyngeal swab (NPS) for SARS-CoV-2 with a high cycle threshold (Ct) of 36.6. Based on this she was deemed non-infectious and was not isolated.

She was investigated as a pyrexia of unknown origin. CT imaging showed bilateral pneumonitis consistent with known recent COVID-19. (Fig.1) All other investigations for infection, connective tissue disease, and malignancy were negative. Multiple repeat NPS for SARS-CoV-2 were negative. She did have hypogammaglobulinemia with decreased IgG, IgA, and IgM.

PET-CT (day 58) showed ground-glass attenuation in both lungs which was more extensive than previous imaging, reflecting active pneumonitis. (Fig.2) A bronchoscopy was performed (day 60) and bronchoalveolar lavage fluid was positive for SARS-CoV-2 with a Ct value of 28.7 suggesting possible active viral replication.

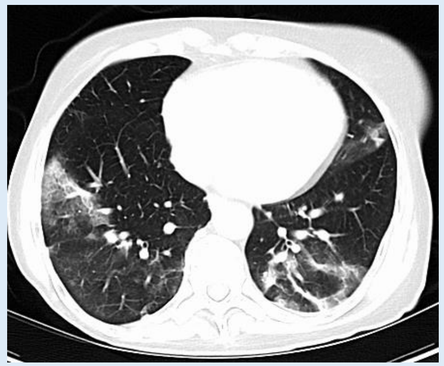

Fig. 1: Bilateral multifocal pneumonitis on initial CT thorax

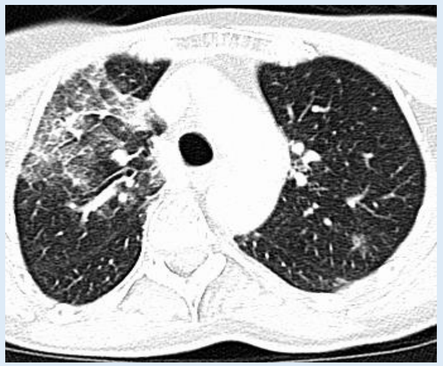

Fig. 2: Interval development of RUL pneumonitis on PET-CT

After exclusion of other causes, the patient's pyrexia was attributed to persistent SARS-CoV-2 infection in the lower respiratory tract. She defervesced after 7 weeks of high-grade fevers and 9 weeks following her diagnosis of COVID-19 (day 65). At day 68 she had no antibodies detectable to either SARS-CoV-2 spike or nucleocapsid proteins.

Despite this patient's persistent high-grade pyrexia she was linked to no onward SARS-CoV-2 transmission during her time in hospital. This could suggest that a febrile patient with potentially active SARS-CoV-2 infection in the lower respiratory tract has a reduced probability of onward virus transmission in the setting of no respiratory symptoms and negative upper airway PCR.

## Conclusion

Patients undergoing rituximab therapy are at risk of prolonged SARS-CoV-2 shedding due to B-cell depletion[1,2]. This can lead to delayed, atypical or prolonged symptoms creating diagnostic challenges and raising difficult infection control questions as illustrated in this case. B-cell depletion also decreases formation of protective antibodies leading to increased risk of reinfection and possible impaired vaccination response[1,2].

## References

1. Yasuda H, Tsukune Y, Watanabe N et al. Persistent COVID-19 Pneumonia and Failure to Develop Anti-SARS-CoV-2 Antibodies During Rituximab Maintenance Therapy for Follicular Lymphoma. Clin Lymphoma Myeloma Leuk. 2020 Nov; 20(11): 774-776. 2. Aydillo T, Gonzalez-Reiche AS, Aslam S, et al. Shedding of Viable SARS-CoV-2 after Immunosuppressive Therapy for Cancer. N Engl J Med. 2020; 383: 2586-2588.

**31/12/20**
Symptom onset

**02/01/21**
NPS SARS-CoV-2 positive In community

**18/01/21**
Pyrexia onset

**01/02/21**
NPS SARS-CoV-2 positive (Ct 36.6)

**03/03/21**
BAL SARS-CoV-2 positive (Ct 28.7)

**08/03/21**
Defervesces

**11/03/21**
No SARS-CoV-2 antibodies detected