Prolonged COVID-19 Infection in a Patient with Multiple Sclerosis and Rituximab-Treatment

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Research Article

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Abstract

We present a prolonged disease course in a 32-year old woman with COVID-19 and multiple sclerosis on rituximab-treatment for three years. The patient was admitted to the hospital for COVID-19 and had persistent fever, cough and radiologic bilateral lung opacities over the course of 29 days. After ineffective antibiotic treatment and the detection that she had no antibodies against SARS-CoV-2 convalescent plasma was administered with rapid recovery ensuing. While there is evidence convalescent plasma is not superior to placebo for COVID-19 in general its role in patients with B-cell depletion and COVID-19 remains to be examined further.

Case:

A 32-year old woman with relapsing-remitting multiple sclerosis (RRMS) presented herself in the emergency unit with fever, coughing, arthralgia and diarrhea for seven days. Multiple sclerosis (MS) was diagnosed 3 years earlier after the patient had developed paresthesia in the left leg and blurred vision. Immunosuppressive treatment with rituximab was established after diagnosis and administered every 6 months, the fifth time two month prior to hospital admission. Since the first course of rituximab no relapses or severe adverse effects occurred.

On presentation the patient was normoxemic and had moderate symptoms. Nasopharyngeal swab was performed and real-time polymerase chain reaction (rt-PCR) tested positive for SARS-CoV-2. Chest x-ray showed bilateral opacities over the lung bases. Elevated C-reactive protein (CRP) was noted (CRP 97.7 mg/L (normal: < 5)) and symptomatic therapy was administered. Since she remained normoxemic no specific antiviral or steroid therapy was administered. Subsequently, the patient was discharged the first time after 4 days with a non-severe course of COVID-19.

Because of persistent cough and fever up to 39,1°C the patient presented herself at the emergency department 15 days after symptom-onset and was admitted to the hospital once more. Rt-PCR for SARS-CoV-2 still tested positive and CRP increased to 176 mg/L. Piperacillin-Tazobactam was initiated for potential bacterial superinfection. Despite this therapy daily fever spikes continued and CRP failed to decrease. Consequently, antibiotic treatment was switched to Meropenem and Vancomycin was added 3 days afterwards but clinical improvement could not be achieved and CRP was continuously high at 200.6 mg/L.

Computed tomography (CT) of the chest (Fig. 1) and abdomen showed persistent bilateral ground glass opacities but no other focus of infection. Transthoracic echocardiogram showed no evidence for endocarditis. Multiple blood cultures and sputum culture showed negative results. In consideration of invasive fungal infections galactomannan and beta-d-glucan were performed with negative results. FACS-analysis showed complete B-cell-depletion but otherwise normal cell population.

25 days after initial symptom-onset rt-PCR tested negative on SARS-CoV-2. Neutralizing antibodies against SARS-CoV-2 were not detectable (electrochemiluminescence immunoassay “ECLIA” - Roche). In

consideration of persistent clinical manifestations of Covid-19 during antibiotic application, failed evidence of other infection and non-detectable SARS-CoV-2-antibodies a treatment attempt with convalescent plasma was initiated lasting 5 days. After the third day of treatment the patient was afebrile the first time since initial symptom onset and sustained clinical recovery ensued. After therapy completion CRP decreased to 35.3 mg/L. Another chest-CT (Fig. 1) showed the bilateral opacities regressive.

Throughout the observed period of time the patient had no signs of activity regarding MS and was finally discharged from hospital 41 days after symptom-onset in good condition.

Discussion:

In this report we described prolonged clinically mild COVID-19 infection after immunosuppressive treatment with rituximab in a patient with multiple sclerosis. Anti-CD20 treatment in multiple sclerosis was shown not to be associated with a higher risk or a more severe course of COVID-19 (1,2). Some reports even suggest a protective role of B-cell depleting therapy for Covid-19. A possible mechanism could be protection from overactive immune responses by immunosuppressive agents (3). Nevertheless, cases of prolonged COVID-19 infection were reported in hematological or rheumatic patients who received B-cell depletion prior to infection. While showing a significantly longer duration of disease activity these cases were not associated with a more severe course (4,5).

Convalescent plasma as a possible therapy approach in B-cell depleted patients with COVID-19 was reported in a case series of 17 patients with no adverse events and favorable outcomes by Hueso et al. (6). However, the recent randomized trial by Ventura et al. showed no different outcomes in COVID-19 patients without immunosuppression treated with convalescent plasma compared to placebo (7). Despite these conflicting results our case report shows that convalescent plasma should be considered for treatment in B-cell depleted patients with COVID-19.

Future trials must determine if the sub-group of immunocompromised or B-cell depleted patients with COVID-19 benefit from convalescent plasma therapy. In addition, the ability to build antibodies is of relevance for potential protective effects of COVID-19 vaccines.

Declarations:

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Figures

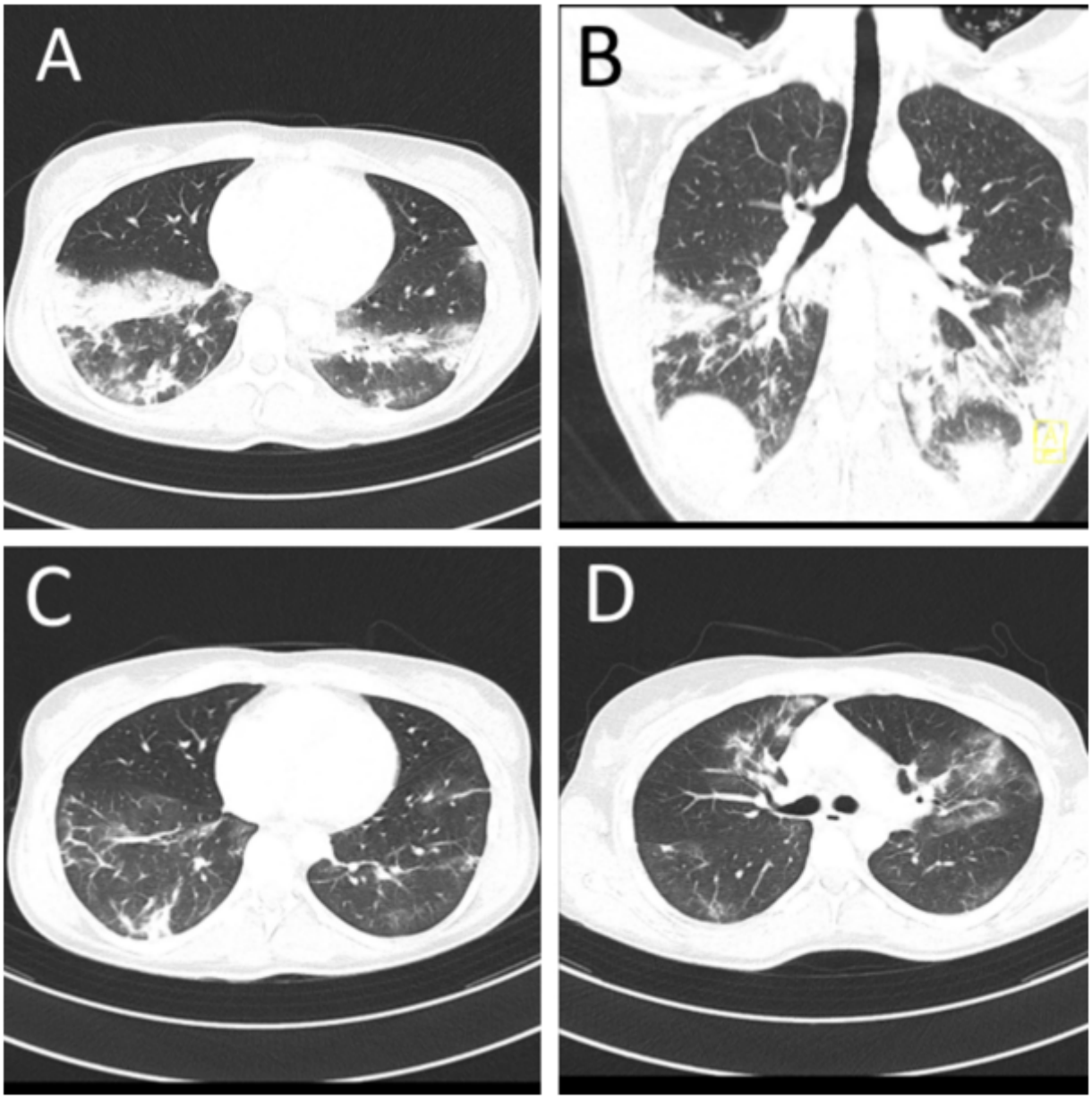

Figure 1

Axial and coronar CT of the chest, on day 19 after symptom-onset (A,B): predominantly lower lobe patchy ground glass infiltration and consolidation with pneumobronchogram in Covid-19 pneumonia and day 35 after symptom-onset (C,D): residual consolidation and considerable improvement of patchy ground glass infiltration