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LETTERS

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Mild course of COVID-19 and spontaneous virus clearance in a patient with depleted peripheral blood B cells due to rituximab treatment

To the Editor:

More than 10 million cases of coronavirus disease 2019 (COVID-19) caused by infection with the novel severe acute respiratory syndrome coronavirus 2 (SARS–CoV-2) have been confirmed worldwide. In up to 20% of cases severe disease develops, and the fatality rate is high (1). However, little is known about the course of the infection in immunosuppressed patients. We therefore report the case of a patient with COVID-19 who was receiving immunosuppression treatment with rituximab (RTX).

The patient, a 77-year-old woman, was admitted to our hospital with a 5-week history of fever of unknown origin (up to 38.5°C), hypotension (systolic blood pressure 80 mm Hg on self-measurement), occasional mild shortness of breath, and intermittent dry cough. Two years prior, she had been diagnosed as having granulomatosis with polyangiitis (GPA) presenting with otitis media, sinusitis, and arthritis, for which she had received repeat courses of RTX. She was currently being treated with prednisone (5 mg/daily) and methotrexate (MTX) (20 mg/weekly). Further medication consisted of folic acid, calcium, vitamin D_3, pantoprazole, rosuvastatin, and zoledronate. Her main comorbidities were Sjögren's syndrome, osteoporosis, and hypercholesterolemia. Two weeks prior to admission, she had begun a 7-day course of amoxicillin and clavulanic acid for presumed sinusitis that, however, had no effect on the fever. Upon admission, clinical examination did not reveal any signs of active GPA. Her body temperature was 37.7°C,

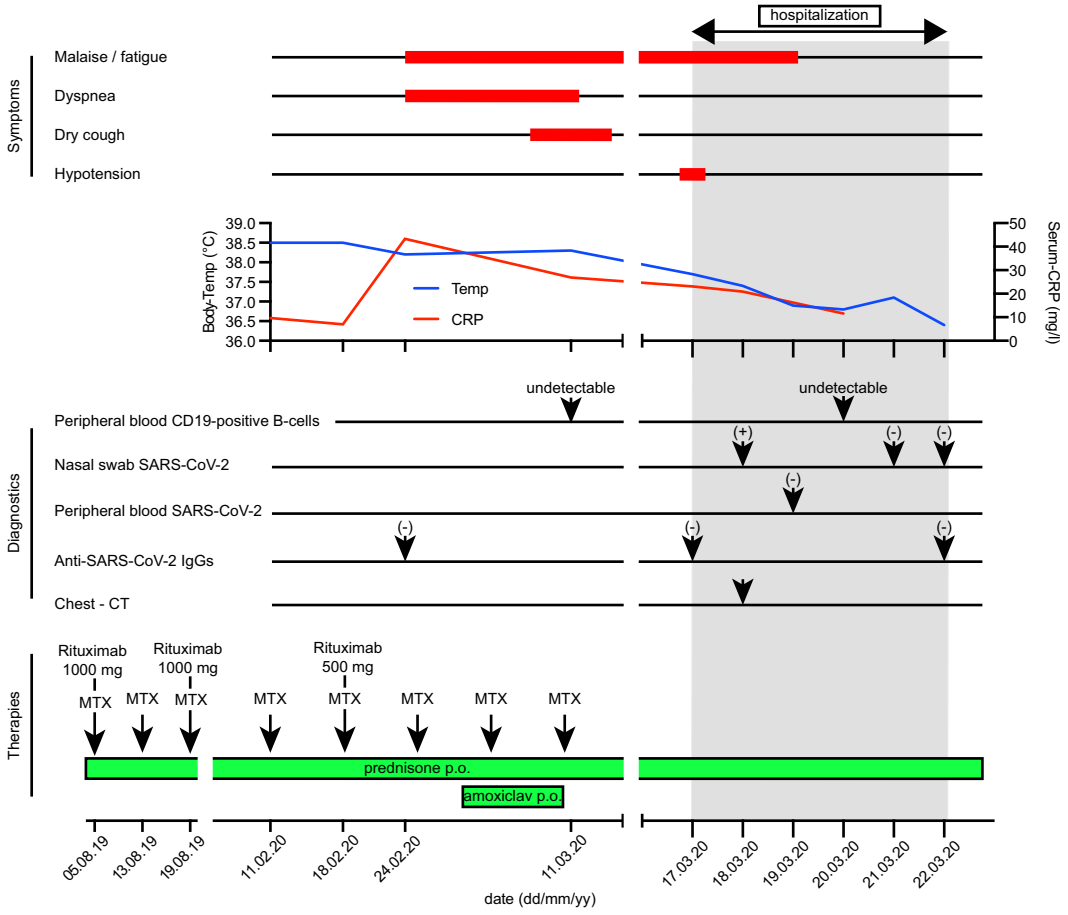

Figure 1. Symptoms at presentation, progression of fever and C-reactive protein (CRP) levels, diagnostic evaluation, and treatments. SARS-Cov-2 = severe acute respiratory syndrome coronavirus 2; CT = computed tomography; MTX = methotrexate; po = by mouth.

respiration rate was 16/minute, peripheral oxygen saturation was 100%, blood pressure was 110/70 mm Hg, and findings on auscultation of the chest were normal. Eye, ear, nose, and throat examination findings were unremarkable; previously elevated titers of proteinase 3 autoantibody had normalized. The B cell compartment in the peripheral blood was completely depleted.

During the subsequent days of hospitalization, the patient continued to experience fatigue and hypotension. The fever and cough had resolved. Computed tomography (CT) of the chest revealed new discrete, bilateral ground-glass opacifications in comparison to CT performed 2 years before, but no other remarkable lung pathology. Nasal swab testing in 2 independent real-time reverse transcriptase–polymerase chain reaction (RT-PCR) tests revealed the presence of SARS–CoV-2 (viral load 149,000 copies/ml). There was no SARS–CoV-2 viremia detected in the peripheral blood using real-time RT-PCR. The patient continued not to require any oxygen supply and remained afebrile. On days 5 and 6 after admission, 2 consecutive nasopharyngeal swabs were SARS–CoV-2 negative, and the patient was discharged. SARS–CoV-2 serologic testing revealed no antiviral IgG (EDI Novel Coronavirus COVID-19 IgG ELISA; Epitope Diagnostics) up to 1 day after virus clearance.

Figure 1 summarizes the clinical course of this elderly patient in whom coronavirus infection was successfully cleared despite a depleted peripheral B cell compartment. The patient, who would commonly be considered at risk for a more severe course of COVID-19 due to her age, immunosuppressive treatment, and proven alveolitis, had only a mild illness. Murine models provide evidence of an important role of T cells in mediating organ damage (2,3), but antiviral IgG also induced severe lung inflammation in a primate model (4). Moreover, serum antiviral antibody levels correlated with disease severity in SARS patients (4,5). Although the magnitude and speed of antiviral antibody response was not associated with COVID-19 severity (6), in our patient, the complete lack of antiviral antibodies might have prevented severe disease. We also cannot exclude the possibility that the additional treatment with MTX played a role in mitigating immune-driven organ damage. Interestingly, the SARS–CoV-2 infection was successfully cleared in this patient independent of specific antibody production. Despite the evidence from murine models that antibodies have a critical role, cellular immunity also plays an important part in virus elimination, and T cell responses to some viral antigens have been shown to remain intact with RTX exposure (3,6,7). In our patient, SARS–CoV-2 was confirmed in 2 independent PCRs, making a false-positive result unlikely. Her body temperature was elevated for >1 month before SARS–CoV-2 detection; it remains unclear whether the fever was due to COVID-19 during this entire period. Her GPA appeared to be completely inactive and was therefore unlikely to have been the cause of the fever. It is also unlikely that the alveolitis seen on CT represents RTX-induced lung edema, given the 4-week lapse between RTX infusion and imaging. Further studies are needed to determine the role of antiviral antibodies and immunosuppression in organ injury and viral clearance of COVID-19.

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Does nonsteroidal antiinflammatory drug use contribute substantially to the osteoarthritis–cardiovascular disease association? Comment on the article by Atiquzzaman et al

To the Editor:

We read with great interest the article by Dr. Atiquzzaman et al describing their study aimed at determining the role of nonsteroidal antiinflammatory drugs (NSAIDs) in the increased risk of cardiovascular disease (CVD) among osteoarthritis (OA) patients (1). Their results demonstrating a mediating role of NSAIDs in the relationship between OA and CVD suggest that NSAID use contributes substantially to the OA–CVD association.

To the best of our knowledge, both OA and CVD are most common among elderly individuals; therefore, we agree that OA patients have a higher risk of developing CVD than controls without OA. However, we have several questions about the following