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Arthritis after SARS-CoV-2 infection

In COVID-19, the pivotal cytokines that provoke severe disease in the lung are similar to those usually targeted by drugs used for treating rheumatoid arthritis. Although COVID-19 is not yet considered as a trigger for rheumatoid arthritis, this similarity has led to the suspicion that COVID-19 might be a risk factor for inducing a rheumatoid arthritis flare.¹ Recently, arthralgia and arthritis have been reported after SARS-CoV-2 infection in three patients that were negative for rheumatoid factor (RF) and anti-citrullinated protein antibody (ACPA).^{2,3} In this Correspondence, we describe a man who developed arthritis after COVID-19.

On February 20, 2020, a 67-year-old non-smoking man attended a routine clinical check-up at the Shymkent Medical Center for Joint Diseases in Shymkent (Kazakhstan). He did not complain of any joint pain or swelling and testing for RF, which was requested as a routine evaluation, was negative. On May 26, 2020, he developed fever, anosmia, shortness of breath, and weakness: chest x-rays showed bilateral interstitial pneumonia (appendix p 1) with 83% oxygen saturation. An RT-PCR for SARS-CoV-2 was positive, and the patient was diagnosed with COVID-19. On June 1, 2020, he was admitted to a provisional COVID-19 hospital in Shymkent (Kazakhstan). After 7 days of treatment with ceftriaxone (1 g per day for 4 days), azithromycin (0.5 g per day for 4 days), and non-steroidal anti-inflammatory drugs (three ibuprofen tablets taken per day when necessary), he was discharged from hospital. On July 2, 2020, he developed morning stiffness (>30 min) and symmetric polyarthritis of the knees and hands (appendix p 2). Testing showed a Disease Activity Score of 28 joints with C-reactive protein (DAS28-CRP)

of 7.35. Furthermore, a high RF concentration (411 IU/mL, normal range <18 IU/mL), a high erythrocyte sedimentation rate (59 mm/h), and a high concentration of CRP (55 mg/L, normal range <5 mg/L) were reported, but ACPA concentration was low (19.2 U/mL, normal range <20 U/mL). A serological anti-SARS-CoV-2 rapid test (COVID-19 IgG/IgM antibody test; Humasis, Anyang, Korea) was positive for IgG and IgA. A diagnosis of early rheumatoid arthritis was made, and treatment with methotrexate (15 mg per week) and methylprednisolone (8 mg per day) was started. After 1 month, the patient's erythrocyte sedimentation rate was 28 mm/h, and the concentration of CRP was reduced but still high (18 mg/L), with a low joint DAS28-CRP of 2.8. An x-ray did not show any parenchymal lesions (appendix p 1), but a chest CT (appendix p 3) detected residual signs of polysegmental pneumonia in the resolution stage, chronic bronchitis, and emphysema. A quantitative serological SARS-CoV-2 antibody test was negative for IgA (0.1 conventional units) but positive for IgG (13.3 conventional units). ACPA concentration was high (104 U/mL). In October 2020, the patient was still receiving treatment with methotrexate and methylprednisolone, was in remission (DAS28-CRP 2.2), and he returned to work.

The patient survived COVID-19 with a standard treatment approach. An association between COVID-19 and the onset of reactive arthritis has been previously postulated.² Approximately 1 month after the resolution of COVID-19 symptoms, the patient developed arthritis with a high RF and, almost 5 months later, a progressive increase of ACPA. However, it is unknown if the persistence of SARS-CoV-2 infection, detected in this patient with the CT via signs of pneumonia in a resolution phase,

could have been a factor triggering the onset of arthritis. Moreover, the response to methotrexate and corticosteroids was satisfactory, with remission of joint disease when the patient was still positive for IgG and IgA anti-SARS-CoV-2 antibodies. This case might suggest that SARS-CoV-2 was involved in triggering RF-positive and ACPA-positive arthritis, which might be diagnosed as rheumatoid arthritis, but we cannot rule out the possibility that the onset of this arthritis could have been coincidental. However, previous reports of the presence of autoantibodies after SARS-CoV-2 infection might suggest that this virus might also act as a trigger of arthritis or other autoimmune diseases.^{4,5} Long-term observation of patients affected by COVID-19 might provide an answer to this challenging question.

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See Online for appendix