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CORRESPONDENCE

Seropositive rheumatoid arthritis after vaccination against SARS-CoV-2 infection

Dear Editor,

Today a frequently asked question is: Can vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) trigger rheumatic and musculoskeletal diseases? Several cases of arthritis have been reported after vaccination against SARS-CoV-2.[1-4] A few articles have investigated the safety of SPUTNIK-V;[5] there is only our one case of arthritis reported after this vaccination.[1] In our *International Journal of Rheumatic Diseases* paper about arthritis after vaccination against SARS-CoV-2[1] we wrote: 'Several patients with rheumatic diseases, treated in the Medical Center of Joint Diseases (MCJD), developed transient flares after receiving the COVID-19 vaccine'. A possible association between rheumatoid arthritis (RA) and influenza vaccination was previously reported in a cohort study;[6] however, there were no cases of seropositive RA after SPUTNIK-V vaccination in the literature. A heterologous recombinant adenovirus-based vaccine, Gam-COVID-Vac (Sputnik V, Gamaleya National Research Centre for Epidemiology and Microbiology), showed a good safety profile and induced strong humoral and cellular immune responses.[5] We would like to present the first case of new-onset seropositive (for rheumatoid factor [RF] and anti-citrullinated protein antibodies [ACPA]) RA after a single dose of SPUTNIK-V vaccine.

We report the case of a 38-year-old Asian non-smoking woman with no history of chronic joint disease, infections, injuries, inflammatory back pain, morning stiffness, or joint swelling. The patient had no previous symptoms of SARS-CoV-2 infection; a serological anti-SARS-CoV-2 rapid test (COVID-19 IgG/IgM antibody test; Humasis,Germany) was negative. The patient received the first dose of the SPUTNIK-V vaccine on May 20, 2021 without developing a fever or adverse events. Twenty days later, pain and stiffness appeared in the left shoulder and 2 days later in the right shoulder, followed by swelling and pain in both knee joints. The patient used non-steroidal anti-inflammatory drugs. She did not visit a doctor nor did she receive the second dose of the vaccine. Two months after vaccination, pain and morning stiffness lasting more than 30 minutes appeared in the small joints of her hands and feet. On August 24, 2021, she underwent an examination at the Medical Centre of Joint Diseases in Shymkent (Kazakhstan). The patient presented morning stiffness for more than 2 hours and symmetric polyarthritis of the knees, feet, and hands. Testing showed a Disease Activity Score of 28 joints with a C-reactive protein (DAS28-CRP) level of 6.02. There were high levels of RF (170 IU/mL, normal range <18 IU/mL), erythrocyte sedimentation rate (39 mm/h), CRP (10 mg/L, normal <5 mg/L), and ACPA (157 U/mL, normal <20 U/mL). The anti-nuclear antibodY (ANA) screen-test and *Chlamydia* and *Ureaplasma* immunoenzyme tests were negative, and the levels of uric acid were normal (241 mmol/L). An immunoenzyme SARS-CoV-2 Spike IgG antibody test had a strongly positive result of 9.81 (0.80 negative, ≤0.80-1.10 borderline, ≥1.10 positive). The positivity coefficient was markedly high at 24.52. Hand X-rays did not show any lesions. Ultrasonography revealed moderate effusion in both knee joints and the metacarpophalangeal and proximal interphalangeal joints of both hands. According to the American College of Rheumatologists/European League Against Rheumatism (ACR/EULAR) classification criteria[7] early RA was diagnosed, and treatment with methotrexate (15 mg per week), non-steroidal anti-inflammatory drugs, and methylprednisolone (100 mg infusion daily for 3 days) was initiated. At the control examination (September 1, 2021) testing showed: CRP 1 mg/L, DAS28-CRP level 3.99, RF 231 IU/mL, and ACPA 314 U/mL.

Two variants of disease development may be considered: a flare of existing RA and a debut of de novo RA. Only two cases of flare RA after COVID-19 vaccination have been reported.[2,3] The first case, mentioned previously,[2] could be explained with the first variant, whereas the second case[3] most likely reflects the second option. In our case, RA pathogenesis could be due to either the first or the second possibility. Unfortunately, the patient was not tested for RF or ACPA before vaccination because she had no previous joint complaints. This woman may have had asymptomatic positive RA, and the COVID-19 vaccination triggered the flare. A rapid increasing of RF and ACPA is significant. We described the rapid growth of ACPA within a month from normal values (18 mg/L) to high values (104 U/mL)[8] in a case of RA that developed after SARS-CoV-2. It is likely that in this case, the vaccination might have been a trigger factor for the rapid onset of RA. It would be appropriate to conduct a genetic study of the patient, as French researchers did;[9] however, similar to other post-vaccine case reports, the causal correlation with RA was not formally established. Nonetheless, we assume that vaccination and SARS-CoV-2 might be trigger factors for

RA, though controlled studies are needed to prove this hypothesis. Analysis of the incidence of RA in different countries over the next 1-2 years is warranted; an increase in incidence in the next 2 years may prove our hypothesis.

KEYWORDS

rheumatoid arthritis, safety of vaccines, severe acute respiratory syndrome coronavirus 2 infection, SPUTNIK-V, vaccination severe acute respiratory syndrome coronavirus 2

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