

## LETTERS TO THE EDITOR

## Progression from palindromic rheumatism to rheumatoid arthritis after COVID-19 vaccination

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Dear editor,

COVID-19 is associated with immune system overactivation, and it is yet unclear if it can lead to autoimmune disease flares. Rare cases of incident rheumatoid arthritis (RA) and reactive arthritis have been reported after COVID-19<sup>1-3</sup>. Other respiratory viral infections including parainfluenza, coronavirus, and metapneumovirus have been associated with incident RA. Rare cases of RA flares have been reported after influenza and hepatitis B vaccinations, but large studies have not reciprocated causality<sup>4-6</sup>.

BNT162b2 and mRNA-1273, both mRNA-based vaccines, and AD26.COV2.S a viral vector-based vaccine, are approved for emergency use in the United States. These vaccines elicit a strong humoral response by viral neutralizing-antibody production, and a strong cellular response by production of proinflammatory cytokines such as interleukin (IL)-2, IL-4, IL-5, IL-13, and interferon- $\gamma$  by CD4+ and CD8+ T-cells<sup>7-9</sup>. It is uncertain if COVID-19 vaccines are associated with flares of the underlying chronic inflammatory disorder (CID) or not. In their clinical trials, patients with autoimmune conditions (such as RA) or those on immunosuppressive medications were excluded. In one study of 26 patients with CIDs, COVID-19 vaccination did not cause disease flares, while a 4% incidence of systemic lupus erythematosus (SLE) flare after COVID-19 vaccinations is reported in the VACOLUP study<sup>10,11</sup>. Theoretically, molecular mimicry leading to autoimmunity may lead to RA flares. However, the American College of Rheumatology deems the benefit of COVID-19 vaccination greater than the potential risk of autoimmunity<sup>12</sup>.

We report the case of a 40-year-old female who presented for rheumatological evaluation. Originally, she presented 7 years ago with episodic monoarticular self-limited (one day) pain and swelling involving hands, wrists and feet. Anti-cyclic-citrullinated-peptide antibody (ACPA) was positive (>250 U/mL), erythrocyte sedimentation rate (ESR), c-reactive protein (CRP),

and radiographs of the hands, wrists and feet were normal. Palindromic rheumatism was diagnosed and hydroxychloroquine 400 mg daily treatment achieved disease remission.

Three months before the current presentation, she received BNT162b2 vaccinations. Two weeks after the second dose, she developed bilateral shoulder stiffness along with pain and swelling of bilateral wrists and hands. Over-the-counter treatment was ineffective and symptoms gradually worsened. On presentation to us, she had tenderness and swelling in bilateral wrists and hands. Shoulder range of motion was reduced with bicipital tenderness. Musculoskeletal ultrasound revealed effusion and synovitis in the radiocarpal joints. Complete blood count and comprehensive metabolic panel were normal and CRP was elevated at 17.2 mg/L. Viral hepatitis B/C panels were negative. Rheumatoid Factor (28 IU/mL) and ACPA (>250 U/mL) were positive. Radiographs of the hands, feet, and shoulders were normal. RA diagnosis was assumed, and methotrexate 15 mg weekly in addition to hydroxychloroquine 400 mg daily was initiated.

Palindromic rheumatism is considered an at-risk phenotype for RA, and progression from the mild intermittent symptoms of palindromic rheumatism to severe persistent symptoms of RA is not uncommon, especially in seropositive patients<sup>13,14</sup>. Thus far, few cases of RA flare after COVID-19 vaccination have been reported, and ours is the first case of progression from palindromic rheumatism to RA after COVID-19 vaccination<sup>15,16</sup>. Autoimmunity triggered by molecular mimicry can be hypothesized as the etiology for this disease progression, although this timing could be coincidental as well. Further research is needed to answer this question. Given the overall safety and efficacy of vaccines for COVID-19, vaccinations in this at-risk population shall be strongly encouraged.

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