Can SARS-CoV-2 infection trigger Rheumatoid Arthritis? A case-report

Sirine Bouzid¹, Saoussen Miladi², ALIA FAZAA², Kawther Ben Abdelghani², and Ahmed Laatar²

¹Charles Nicolle Hospital
²University Hospital Center Mongi Slim

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Abstract
A 38-year-old female developed chronic joint pain one month after testing positive for SARS-CoV2. Physical examination revealed warmth and tenderness of the wrists and small joints of the hands. Rheumatoid factor and anti-CCP were elevated. Hands MRI showed synovitis of small joints. The patient was diagnosed with rheumatoid arthritis (RA).

Introduction
Coronavirus disease 19 (COVID-19) is a viral infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). An increase in pro inflammatory cytokines (IFN-γ, IL-1, IL-6, IL-12, and TNF-α) and chemokines (CCL2, CXCL10, CXCL9, and IL-8) described as a cytokine storm or hyperinflammatory syndrome may develop during the course COVID-19 (1).

Cases of autoimmune disorders presenting or exacerbating after SARS-Cov-2 infection have been reported (2). Herein, we report the first case of Rheumatoid arthritis occurring one month after COVID-19 infection.

Patient and observation

Patient Information: We report the case of a 38-year-old female with no significant medical history.

Clinical Findings: She presented with chief complaints of 4 months of progressively worsening pain of her small hand joints, wrists, knees, and ankles symmetrically. She also complained of morning stiffness lasting two hours and was exhausted throughout the day. Symptoms begun one month after a COVID-19 infection confirmed by a positive throat swab. The infection was mild; the patient only experienced symptoms of cough, fever, chills, without arthralgia and did not need hospitalization nor oxygen therapy.

She did not report any fevers, chills, night sweats, weight loss or rash upon presentation. She had no history of joint problems, gonorrhea, chlamydia, diarrhea, or uveitis. She denied alcohol use or smoking cigarettes. Her maternal aunt has Rheumatoid Arthritis.

Diagnostic assessment: Initial laboratory workup included a complete blood count which was within normal limits, ESR of 13 mm, and CRP of 4,3 mg/L. Immunological workup revealed elevated antinuclear antibodies titer (1:640), negative ENA and dsDNA antibodies, positive rheumatoid factor measured by ELISA (62,29) and positive anti-cyclic citrullinated peptide (anti-CCP) antibodies (237,39). Serology tests for hepatitis B virus and hepatitis C virus were negative. Joint x-rays including wrists, hands, knees, ankles, feet showed no evidence of erosions. Hands Ultrasound did not reveal any signs of synovitis.
Hands MRI showed synovitis of both distal radio-ulnar joints and metacarpophalangeal joint of the left second compartment. It also showed inflammation around extensor carpi ulnaris tendons with synovial enhancement of the tendon sheaths suggestive of tendonitis. No adjacent osseous destruction was found.

**Diagnosis:** Although our patient presented with inflamed joints one month after a viral infection (COVID-19), it is less likely to be a reactive arthritis since she presented with chronic and symmetric polyarthritis of small and large joints without increased inflammatory markers (ESR and CRP) and had positive anti-CCP antibodies.

Our patient meets the formal criteria for the diagnosis of Rheumatoid Arthritis according to the current ACR/EULAR 2010 criteria: joint involvement of more than 10 joints for a period of more than 6 weeks with high positive ACPA. No striking extra-articular signs or symptoms were found to suggest a different systemic immune disease such as systemic lupus erythematosus (SLE). Disease activity was moderate with a DAS28-ESR of 4.6.

**Therapeutic interventions:** Treatment was initiated with methotrexate and non-steroidal anti-inflammatory drugs.

**Follow-up and outcome of interventions:** After treatment, an improvement of the symptoms as noted with a DAS28 ESR after 2 and 5 months at 3.7 and 3.1, respectively

**Informed Consent:** The patient gave her consent for publishing her case with absolute respect of anonymity.

**Discussion**

To our knowledge, this the first case of RA triggered by COVID-19 infection. RA is an immune-mediated disease which etiopathogenesis involves genetic predisposition, environmental and hormonal factors. Ambient respiratory viral infections are suggested to be associated with an increased incidence rate of RA after a moderate time interval (3). In an ecological study, Coronavirus was among the viruses most associated with the number of incident RA (3).

Since the emergence of COVID-19, only few cases of reactive arthritis post SARS-CoV-2 infection have been reported. This low frequency can be explained by the use of corticosteroids in the treatment of this viral infection (4). All cases reported were man and joint inflammation affected lower extremities and occurred approximately 12 to 32 days after COVID-19 diagnosis (4). However, reactive arthritis remains a diagnosis of exclusion in all these cases.

The development of rheumatological diseases such as systemic lupus erythematosus (SLE), following the infection with SARS-CoV-2 has been described (2). Most cases reported were women with a median age of 43 years (range 18–85) (2). SLE was suspected when severe complications occurred such as severe thrombocytopenia, serositis and kidney damage which were not related to the severity of the respiratory disease. Glucocorticoids alone or in association with hydroxychloroquine were used as the first line of treatment (2).

Infections can activate the innate immune system leading to the production of autoantibodies, either through an aberrant response or lack of immune control. This mechanism is implicated in the pathogenesis of SLE (5). In a meta-analysis, patients (n=120) hospitalized for COVID-19 underwent immunological workup, the prevalence of ANA and RF were 32.1% and 19.9%, respectively (6). Other autoantibodies have also been reported but at lower frequencies; 5.46% for anti-CCP antibodies (6–8).

This highlights the ability of SARS-CoV-2 to trigger autoimmunity phenomena. This effect is caused by the ability of this virus to induce hyper-stimulation of the immune system and its molecular similarity to humans (9).

**Conclusion**

We report the first case of RA starting one month after a Covid-19 infection. Further documentations are needed to comprehend the link between SARS-Cov-2 and auto-immune diseases and particularly RA.
Competing interests
The authors declare no competing interest.

Authors’ contributions
- Sirine Bouzid has drafted the work
- Kaouther Ben Abdelghani has substantively revised the work
- Saousen Miledi and Alia Fazaa have made substantial contributions to the literature research
- Ahmed Laatar has made substantial contributions to the conception of the work

References