Case Report



# New onset systemic lupus erythematosus after COVID-19 infection: a case report

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**Abstract:** COVID-19 is a respiratory viral illness that can have life threatening complications. While the short-term sequela of COVID-19, including cytokine storm, is relatively well known, the long-term complications of COVID-19 infection on the immune system is still unknown. There have been some reported cases of autoimmune disease development after COVID-19 infection. We present a patient with a history of COVID-19 infection one month prior who presented with non-specific symptoms including fatigue, malaise, bilateral lower extremity swelling and shortness of breath. His laboratory evaluation and physical exam showed him to be in acute renal failure. Further workup and kidney biopsy results confirmed systemic lupus erythematosus (SLE). Our patient needed treatment with plasmapheresis and immunosuppressants, and subsequently had significant improvement in his symptoms. We discuss the current 2019 European Alliance of Associations for Rheumatology/American College of Rheumatology (EULAR/ACR) diagnostic criteria for SLE and describe plausible mechanisms of COVID-19 induced lupus such as B-cell activation by the virus. We also explore the role of interferons in the potential development of autoimmune diseases after COVID-19 infection and highlight the need for further research in the area.

**Keywords:** Systemic lupus erythematosus (SLE); COVID-19; autoimmunity after infection; case report

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## Introduction

COVID-19 is a viral illness that has been associated with pulmonary edema, acute respiratory distress syndrome and rise in several inflammatory markers. The cytokine storm associated COVID-19 infection is an area of active ongoing research. Due to the recency of COVID-19, long term effects of the disease are still unknown. There have been several case reports of neurologic changes, skin findings, pancreatic disease, and musculoskeletal manifestations after COVID-19 infection. We present the case of a patient who developed systemic lupus erythematosus (SLE) one month after mild COVID-19 infection. We present the following case in accordance with the CARE reporting checklist (available at https://acr.amegroups.com/article/view/10.21037/acr-21-55/rc).

## Case report

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the editorial office of this journal.

A 53-year-old male with a past medical history of essential hypertension, chronic kidney disease 3 and prior COVID-19 pneumonia, one month prior to admission who was treated conservatively at that time with self-isolation,

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presented to the hospital with multiple generalized complaints. His complaints included persistent fatigue, malaise, wrist pain, intermittent nausea and vomiting, exertional dyspnea, bilateral lower extremity swelling and decreased urine output. His surgical history was significant for prior cholecystectomy at age 30. His family history was significant for hypertension and diabetes in both mother and father, but no family history of autoimmune diseases. He was a non-smoker, drank alcohol socially (one to two beers once a month or so) and denied any recreational drug use. Vitals were all normal on admission. Physical exam revealed diffuse synovitis involving most MCPs and PIPs, bilateral wrists, elbows, and bilateral ankles, highly suggestive of SLE. His chronic kidney disease was presumed to be from uncontrolled hypertension and no prior biopsies were done. Initial work-up was notable for elevated creatinine at 7.1 mg/dL from a prior stable baseline of 1.4 mg/dL and nephrotic-range proteinuria with urine protein to creatinine ratio of 14.2. Hemoglobin A1c was 5.4%. TSH was normal at 2.5 mIU/mL. Chest X-ray showed bilateral pleural effusions and vascular congestion. An echocardiogram showed normal ejection fraction of 65% without any diastolic dysfunction or wall motion abnormalities. Labs were significant for antinuclear antibody (ANA) elevation at 1:1,280 with speckled pattern on reflex staining. Double stranded DNA was elevated at 150 IU/mL. Anti-histone, anti-Ro, anti-La, anti-Scl70, anti U1RNP and anti-glomerular basement antibodies were all negative. Anti-neutrophilic cytoplasmic antibody was <1:20. C3 and C4 levels were decreased at 40 and 6 mg/dL, respectively. Renal biopsy demonstrated focal segmental glomerulosclerosis, a collapsing variant. The light microscopy revealed mild podocyte hyperplasia and increase in mesangial cellularity and matrix. Severe interstitial fibrosis and tubular atrophy involving 70–80% of the cortical parenchyma with focal dense inflammation was also noted. Electron microscopy revealed glomeruli with global sclerosis and intracapillary deposits. The patient was classified as having stage IV lupus nephritis. Due to patient's prior history of COVID-19 illness and case reports of COVID-related podocytopathy, COVID-19 staining was completed but found to be negative (1).

Given his lab findings and clinical presentation, his renal pathology was attributed to SLE and he was initiated on methylprednisolone 1 gram daily for 3 days and then transitioned to oral prednisolone 60 mg, along with plasmapheresis (6 rounds) and mycophenolate and hydroxychloroquine. Towards the end of the hospitalization, patient's renal function began to trend toward improvement from a peak creatinine of 10.96 to 8.79 mg/dL at the time of discharge with improved urine output. His C3 and C4 levels prior to discharge were 90 and 25 mg/dL, respectively. At the time of discharge his immunosuppressant regimen included prednisolone 30 mg twice a day, hydroxychloroquine 200 mg twice a day and mycophenolate180 mg twice a day.

Two months after discharge, patient reported significant improvement in his symptoms overall. His creatinine was 4.6 mg/dL with moderate urine output. He was on scheduled hemodialysis three days a week. At that time, patient was thankful for the care he had received throughout his hospital course and in the outpatient setting. He stated that the hospital staff were able to comfort him and reassure him at a very terrifying time for him. He was optimistic about being able to eventually stop hemodialysis and hopeful for full kidney function recovery.

## Discussion

Although extremely rare, autoimmune diseases can develop after COVID-19 infection (2). However, cases of SLE specifically after COVID-19 are uncommon. Only two cases of SLE manifesting after COVID-19 infection have been noted in literature. The first case report was reported from Iran and the second one was reported in Italy (3,4). We report the case of a patient who developed SLE and lupus nephropathy one month after COVID-19 infection. Our patient needed multiple plasmapheresis and several immunosuppressive medications to control his lupus associated symptoms.

Our patient was diagnosed with SLE using the 2019 EULAR/ACR criteria. The first step in EULAR/ACR criteria involves measuring the ANA. If the ANA levels are not greater than 1:80, then it is not classified as SLE. If the ANA levels are greater than 1:80, then a weighted scoring system, including clinical domains as well as immunological domains, is used. The clinical domains include constitutional, neuropsychiatric, mucocutaneous, serosal, musculoskeletal, and renal. Immunologic domains used in the criteria are antiphospholipid antibodies, complement proteins and SLE-specific antibodies. A total score of 10 or more leads to a diagnosis of SLE (5). Our patient had ANA level was 1:1,280. Our patient's joint involvement, proteinuria, low C3 and C4 levels and presence of anti-ds DNA antibodies yielded 20 points and a subsequent diagnosis of SLE. Moreover, our patient also had class IV

lupus nephritis findings on biopsy. The presence of ANA and lupus nephritis also will satisfy the diagnosis of SLE.

The mechanism behind the development of autoimmune disease after COVID-19 infection remains unclear. But recent studies have shown that patients that are critically ill from COVID-19 infection have increased B-cell activation. The B-cell activation results in increased antibody secreting cell lines resulting in increased immune responses, like patients with autoimmune diseases (6). The induction of autoimmune antibodies and B cell activation was also observed when comparing unexposed individuals, patients with mild COVID-19 symptoms and patients with COVID-19 who developed acute respiratory distress syndrome (7).

Interferons could also potentially play a key role in the development of autoimmune diseases after COVID-19 infection. Interferons play crucial role in producing adequate response to pathogens and damaged cells in the body. Interferons are divided into three separate types, Type I, II and III based on the structure and the receptor associated with them (8). Type I interferons, such as IFN-α and IFN-β, affect the release of pro-inflammatory cytokines and are often induced by viruses (9). Type I interferon responses seem to be heavily increased in COVID-19 infections (10). Many patients with autoimmune diseases, such as SLE, also have increased expression of IFN-α (11). Further studies need to be conducted to link potential connection between Type I interferons, COVID-19 and development of autoimmune diseases.

Viral activation of autoimmune diseases is not unique to COVID-19 and has been seen in other viral illnesses. EBV and other herpes associated SLE cases have been reported extensively in the Filipino population (12). There also have been several cases highlighting the association between hepatitis C and SLE (13). Correlation between parvovirus and autoimmune diseases including SLE, rheumatoid arthritis, Hashimoto's thyroiditis and myasthenia gravis have been documented (14).

Another possibility is that the patient already had underlying SLE that was undiagnosed, and patient had a flare up after his COVID-19 infection. However, our patient's creatinine had been stable at 1.4 mg/dL for several years prior to the admission and patient denied any fatigue, rash or joint pains prior to admission. Moreover, patients with systemic autoimmune diseases have been noted to have more severe infection with COVID-19 (15). The exact reasoning behind the increased severity of COVID-19 infection in patients with autoimmune disease is still unclear. One possible mechanism has to do with the of the rise in inflammatory makers in COVID-19. In patients with already heightened immune responses, such as those with systemic autoimmune diseases, the immune response to pro-inflammatory markers becomes further disproportional leading to a heightened state of COVID-19 infection. Our patient, however, only had minor symptoms with COVID-19 infection. He never became hypoxic and was treated with self-isolation and increased oral intake only. Our patient's lack of severe acute immune response with the COVID-19 infection also makes an association between COVID-19 and his subsequent SLE likely.

## Conclusions

In conclusion, we report the first case of post COVID-19 SLE in the United States of America. COVID-19 is still a novel disease, and the long-term manifestations of COVID-19 are still unclear. There seems to be a link between autoimmune diseases and COVID-19. The exact mechanism behind such a connection is still unknown and is an area that will benefit from continued research.

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## Footnote

*Reporting Checklist:* The authors have completed the CARE reporting checklist. Available at https://acr.amegroups.com/article/view/10.21037/acr-21-55/rc

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised

in 2013). Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the editorial office of this journal.



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