Onset of Remission Following COVID-19 Infection in a Patient with Refractory Lupus Nephritis

Dear Sir,

The COVID-19 pandemic has raised several concerns for patients with systemic lupus erythematosus (SLE). Data from the COVID-19 Global Rheumatology Alliance registry indicate that intake of prednisolone ≥10 mg/day is associated with a higher odds of hospitalization for COVID-19 − affected rheumatic patients.[1] There are reports connecting SLE flare with COVID-19[2] and of *de novo* diagnosis of SLE following COVID-19.[3] Host's ability to mount antiviral response with attendant viral clearance, duration of viral shedding, and antibody response in the background of immunosuppression are other major concerns. While there are previous reports of SLE flare following COVID-19, we report quiescence of SLE activity in a patient with refractory lupus nephritis and central nervous system involvement following COVID-19.

A 21-year-old lady presented with Class IV lupus nephritis in May 2020. Mycofenolate was excluded due to severe gastrointestinal intolerance, and lupus nephritis was refractory to cyclophosphamide induction and culminated in crescentic glomerulonephritis in March 2021, necessitating temporary hemodialysis. She then manifested leukopenia and central nervous system symptoms like persistent headache and status epilepticus. Rituximab (2 g total) and four sessions of plasmapheresis were instituted. Her renal function improved and she became dialysis independent; her serum creatinine stabilized at 2.3 mg/dl. However, headache, leukopenia, and hypocomplementemia persisted even after rituximab and plasmapheresis. The SLE disease activity index year 2000 (SLEDAI 2K) score following plasmapheresis and rituximab remained high at 37, indicating active SLE. In April 2021, she developed fever and was diagnosed with COVID-19 based on reverse transcription-polymerase chain reaction (RT-PCR) testing. She was hospitalized and treated with remdesivir, thromboprophylaxis, and dexamethasone; she recovered well from COVID-19 after a mild illness that lasted for 2 weeks. While recovering from COVID-19, the patient had complete resolution of headache, normalization of serum complement level, resolution of leukopenia and erythrocyturia, and the SLEDAI 2K score declined to 4 [Table 1]. She continued to be in remission till the last follow-up in August 2021. She had residual subnephrotic proteinuria and low estimated glomerular filtration rate (eGFR) that could be ascribed to fibrous crescents in biopsy. On day 30 following COVID-19 onset, nasopharyngeal swab RT-PCR tested negative, while antibody to spike antigen remained undetectable.

This patient had active lupus with renal, hematologic and central nervous system involvement that defied

Table 1: Clinical course of SLE and COVID-19 on a timescale

Month	1	2	3	4	5	6	7	8	9	10	11	12	13-16
Ailment	SLE, class IV LN, active lupus with worsening proteinuria, lupus headache, skin rash, MMF-induced hemorrhagic gastritis, steroid-induced diabetes mellitus, diabetic ketoacidosis, hypertension										Renal flare, leukopenia Status epilepticus, lupus head ache	COVID-19 (Mild), AKI	SLE remission
Urine PCR g/g	1.3	1.2		2.0		2.7	3.6	4.5	4.8		5.2	3.7	0.5
Urine erythrocytes	3+	3+		2+		3+	3+	2+	3+		3+	1+	Nil
Creatinine mg/dl	1.0	0.8	0.7	0.6	0.8	0.8	0.8	0.7	1.0	1.8	6.7	2.3-3.7	1.8
eGFR ml/min/1.73 m^2	80.5	105	124	130	105	105	105	124	80.5	39.5	8.1	28.4-16.5	39.5
Kidney biopsy	Class IV LN										TMA crescent-fibrous & cellular		
WBC count Cells/mm^3	14,000	12,100	15,000	13,300	7800	10,600	5780	6500	4800	2500	2100	13,700	11,600
C3 mg/dl	56				64				48				100
C4 mg/dl	5				8				2				28
SLEDAI 2K	30										37		4
Treatment	MMF PDN	Monthly Intravenous cyclophosphamide – 750 mg×7 doses PDN 30 mg/day to 15 mg/day Hydroxychloroquine									Hemodialysis Rituximab 2 g total Apheresis four sessions	Dexamethasone Remdesivir, anticoagulant	PDN 10 mg/day

AKI = acute kidney injury, C3 and C4 = complement components, eGFR = estimated glomerular filtration rate expressed as ml/min/1.73 m^2, LN = lupus nephritis, MMF = mycofenolate mofetil, PCR = protein creatinine ratio, PDN = prednisolone, SLE = systemic lupus erythematosus, SLEDAI 2K = SLE disease activity index year 2000, TMA = thrombotic microangiopathy, WBC = white blood cells

intense immunosuppression including rituximab and plasmapheresis. She entered into remission following COVID-19 illness. Since this patient had received intense immunosuppressant therapy including rituximab and plasmapheresis just preceding COVID-19, it cannot be argued that COVID-19 and the onset of SLE remission are connected. However, it is evident that SLE did not flare after COVID-19 and that there is scope for remission of SLE following COVID-19.

Comorbidities like diabetes, hypertension, and obesity are determinants of adverse outcomes with COVID-19 in rheumatic patients, similar to those in the general population.[4] Patients with rheumatic disease and COVID-19 could be at a higher risk of requiring mechanical ventilation and admission to intensive care unit compared to patients not having rheumatic disease.[5] Glucocorticoid use for rheumatic disease has been found to be associated with hospitalization for COVID-19.[6] This patient had several risk factors for adverse outcome, including diabetes mellitus, hypertension, and prednisolone intake >10 mg/day. However, she had a mild COVID-19 without any hypoxia or necessity for admission to intensive care unit. The United States Food and Drug Administration has approved remdesivir for all hospitalized patients irrespective of the severity of COVID-19 illness, and this patient received a 5-day course of remdesivir since she had several risk factors for adverse outcome. She made a good recovery from COVID-19. Heightened interferon activity in the context of active lupus is postulated to exert a protective antiviral effect.[7] The patient had prolonged viral shedding and blunted antibody response to COVID-19, which could be explained by the background immunosuppression.

While there is a concern that SLE could flare following COVID-19, this case highlights that there could be remission of disease activity following COVID-19.

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Conflicts of interest

There are no conflicts of interest.

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