A Case of Systemic Lupus Erythematosus Flare Triggered by Severe Coronavirus Disease 2019

To the Editor:

We report a case of systemic lupus erythematosus (SLE) flare with hematological manifestations consistent with Evans syndrome, likely precipitated by coronavirus disease 2019 (COVID-19).

CASE PRESENTATION

A 62-year-old man presented to our emergency department with cough, shortness of breath, headache, and a diffuse purpuric rash for 1 week. He had a temperature of 37.1°C, heart rate of 103 beats/min, blood pressure of 159/85 mm Hg, and oxygen saturation of 88% on room air. Physical examination was unremarkable except for the diffuse purpuric rash.

He had a prior medical history of diabetes mellitus and SLE with musculoskeletal (bilateral inflammatory hand arthritis) and hematological (mild thrombocytopenia) involvement. He received the diagnosis 3 weeks prior to his admission and was positive for antinuclear antibodies in a homogenous pattern at a titer of greater than 1:160 and anti–double-stranded DNA at 41 IU/mL. Rheumatoid factor was also positive at 24 IU/mL. Anti-Smith, antiribonucleoprotein, anti-SSA, anti-SSB, anti–cyclic citrullinated peptide, anti–proteinase 3, and antimyeloperoxidase antibodies were negative. He was not started on therapy at that time for unclear reasons.

Laboratory work on admission revealed a normocytic anemia with a hemoglobin of 9.1 g/dL, thrombocytopenia with a platelet count of 2000 cells/μL, and predominantly indirect hyperbilirubinemia with an indirect bilirubin of 2.9 mg/dL. Coagulation panel was remarkable for a mildly prolonged prothrombin time to 15.4 seconds, prolonged activated partial thromboplastin time to 41.8 seconds, elevated fibrinogen to 561 mg/dL, and an elevated D-dimer to 1.46 fibrinogen equivalent units. C-reactive protein was 11.90 mg/dL. Antiphospholipid serology was positive for lupus anticoagulant, anticardiolipin, and anti–β2-glycoprotein antibodies. Complement 3 and complement 4 levels were low. He was negative for human immunodeficiency virus and hepatitis viruses. Kidney function was normal, and a peripheral smear did not reveal any schistocytes or clumped platelets but did show spherocytes and giant platelets.

A chest x-ray revealed bilateral patchy airspace opacities. Computed tomography of the head revealed an intraventricular hemorrhage in the lateral ventricles, which was stable throughout his admission. He was admitted to the intensive care unit for severe thrombocytopenia and intraventricular hemorrhage requiring frequent transfusions and neurological examinations. He tested positive for COVID-19 and was enrolled in a remdesivir trial. He received a total of 10 doses of remdesivir.

A clinical diagnosis of immune thrombocytopenia was made. He was started on dexamethasone 40 mg daily for 4 days and intravenous immunoglobulin 1 mg/kg daily for 5 days. The etiology of his anemia was found to be immune-mediated hemolysis as his haptoglobin was low (<6 mg/dL), and direct Coombs test was positive for immunoglobulin G and complement 3, suggestive of warm and cold antibody-mediated immune hemolysis.

The patient's acute hypoxemic respiratory failure progressively worsened despite supplemental oxygen through a nonrebreather mask, and he was eventually intubated on day 11 of his admission. Given Evans syndrome refractory to first-line therapy, he was started on a rituximab infusion. On day 13 of admission, he became hypotensive requiring vasopressors to maintain his blood pressure. He did not have any interval increase in his leukocyte count, bandemia, or C-reactive protein since day 11 of admission to suggest infection or worsening inflammation, and he did not have any other organ failure, which could account for his clinical deterioration. Blood, endotracheal aspirate, and urine cultures drawn at this time were negative. On day 14, he became progressively hypotensive and bradycardic and died of progression of his illness.

DISCUSSION

Systemic lupus erythematosus is a chronic, systemic autoimmune condition characterized by a myriad of clinical presentations in the setting of positive antinuclear and other autoantibodies. A lupus flare involves new or worsening clinical signs, symptoms, and/or laboratory values involving 1 or more organ systems.[1] Several factors have been implicated to induce a lupus flare. Triggers include noncompliance or tapering of medications, pregnancy, hormones, and infections.[2] Activation of the innate immune system by infections leading to the production of autoantibodies, either through an aberrant response or lack of immune control, has been implicated in the pathogenesis of SLE.[3] Among viral infections parvovirus B19, herpes-zoster virus, and cytomegalovirus have been implicated.[4] To our knowledge, this is the first reported case of SLE that has flared because of COVID-19 infection. Coronavirus disease 2019 has been reported to trigger other autoimmune diseases such as immune thrombocytopenia.[5]

A case of acute respiratory distress syndrome due to COVID-19 following rituximab infusion has been reported.[6] It was postulated that immunomodulatory agents, such as rituximab, may be beneficial and may have delayed time to mechanical ventilation by limiting cytokine storm. However, rituximab, a monoclonal antibody targeted against the CD20 antigen, is cytotoxic to the B lymphocytes, thereby reducing the production of antibodies. This may impair the antibody response to infections, including COVID-19, resulting in clinical deterioration of critically ill patients.[7] Furthermore, rituximab has been reported to result in cytokine release syndrome.[8] Although it is difficult to pinpoint rituximab as the cause of our patient's decline, the temporal association and rapidity of his clinical deterioration make a strong argument for this. Immunomodulatory agents such as steroids, interleukin 6 inhibitors, and interleukin 1 inhibitors are currently being assessed in clinical trials for safety and efficacy in COVID-19.[9] However, given the paucity of data, there is clinical equipoise in determining when to use immunomodulatory therapy.

Sairam Raghavan, MD
Sriram Gonakoti, MD
Iriagbonse Rotimi Asemota, MD
Benjamin Mba, MD, MRCP, FACP
John H. Stroger Jr. Hospital of Cook County Chicago, IL
sairam.raghavan@cookcountyhhs.org

The authors declare no conflict of interest.

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