


COVID-19 and Acute Lupus Pneumonitis: Diagnostic and Treatment Dilemma

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Abstract

In this article, we present a case of a young female patient with previously diagnosed lupus pneumonitis, now with a flare and new superimposed COVID-19 infection that was treated with intravenous steroids. On computed tomography scans, she had extensive interstitial lung fibrosis in addition to a positive COVID-19 polymerase chain reaction test requiring 6 L of oxygen via nasal cannula on admission. After administration of methylprednisolone, the patient improved and was weaned off her oxygen requirements and was discharged home.

Keywords

COVID-19, lupus, pneumonitis, pneumonia

Case Report

A 22-year-old female with a past medical history of systemic lupus erythematosus (SLE), which included fibrotic lupus pneumonitis, grade IV lupus nephritis, and pericardial tamponade, presented to the hospital due to fevers and progressive shortness of breath. Initial oxygen saturations on room air were in the low 80s. A computed tomography (CT) scan of the lungs showed granular and interstitial ground glass opacities with chronic interstitial lung fibrosis (Figure 1). At presentation, the differential diagnosis included an acute exacerbation of chronic lupus pneumonitis and COVID-19 interstitial pneumonia. As a result, the first test performed was a COVID-19 polymerase chain reaction (PCR) test. To evaluate for an acute lupus flare, anti-dsDNA and C3/C4 serum complement levels were ordered, which showed anti-dsDNA at 19 IU/mL (reference interval: <10 IU/mL). Serum complement levels C3/C4 were mildly decreased at 84 mg/dL and 9 mg/dL, respectively (reference interval: C3 [88–201 mg/dL]; C4 [10–40 mg/dL]). Additionally, proteinuria was not detected on urinalysis. Other initial laboratory findings showed lymphopenia, elevated D-dimer levels, elevated lactate dehydrogenase (LDH) levels, and a negative upper respiratory PCR viral panel. Atypical pneumonia sputum culture was also negative. The patient's home medications including hydroxychloroquine and mycophenolic acid as a part of her outpatient management of SLE were continued. Due to the diagnostic dilemma between acute lupus pneumonitis and COVID-19 interstitial pneumonia, the patient was not given any steroids initially. The patient required up to 6 L of oxygen

via nasal cannula, maintaining an oxygen saturation of 94%. After 24 hours of admission with no improvement, the patient was started on 60 mg of intravenous methylprednisolone 3 times daily, which resulted in improved respiratory status and decreased oxygen requirements to 2 L via nasal cannula to maintain oxygen saturation of 94%. Eventually, results of the COVID-19 PCR test returned as positive. On day 5 of her hospital admission, the steroids were tapered down to a total 60 mg of oral prednisone daily, and a repeat CT scan showed significant improvement (Figure 2). The patient was subsequently removed from the nasal cannula with an oxygen saturation of 95% on room air and was discharged home.

Discussion

Lupus Pneumonitis

Pulmonary manifestations are very common in patients with SLE, with 50% to 70% of patients suffering from some form of pulmonary complication during the disease process.¹

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Figure 1. Computed tomography scan showing granular and interstitial ground glass opacities.

These pulmonary manifestations may include pleural disease such as pleurisy or pleural effusions, parenchymal disease, vascular involvement including pulmonary arterial hypertension, diffuse alveolar hemorrhage, and venous thromboembolism, as well as superimposed infections.¹ Acute lupus pneumonitis is a relatively rare pulmonary complication, only occurring in 1% to 4% of patients with SLE.^{1,2} The presenting symptoms of patients with acute lupus pneumonitis are relatively nonspecific, and therefore are difficult to distinguish from infectious etiologies or acute respiratory distress syndrome (ARDS).³ In one case series, the most common presenting symptoms of lupus pneumonitis included fever, cough, dyspnea, hypoxia, and lung crepitations.³ This is consistent with our patient, as she presented with fevers and progressive dyspnea. Mortality of patients with acute lupus pneumonitis is notoriously poor with rates up to 50%.^{1,4} A large percentage of patients who survive acute episodes of lupus pneumonitis will progress to chronic interstitial pneumonitis^{1,4} as in our patient. Because of the nonspecific symptoms at presentation and the relatively high mortality rate, one can appreciate the necessity of prompt initiation of treatment in patients whom this condition is suspected.

Laboratory abnormalities are common in patients with lupus, and in fact hematologic abnormalities including hemolytic anemia, leukopenia, lymphopenia, or thrombocytopenia are included in the 2019 classification criteria for SLE by the European League Against Rheumatism/American College of Rheumatology.⁵ Additional abnormalities often include antibodies against double-stranded DNA, Smith antigen, RO/SS-A, La/SS-B, and nuclear ribonucleoprotein.² Findings on radiography and histology in patients with lupus pneumonitis tend to be nonspecific as well. Chest radiography often

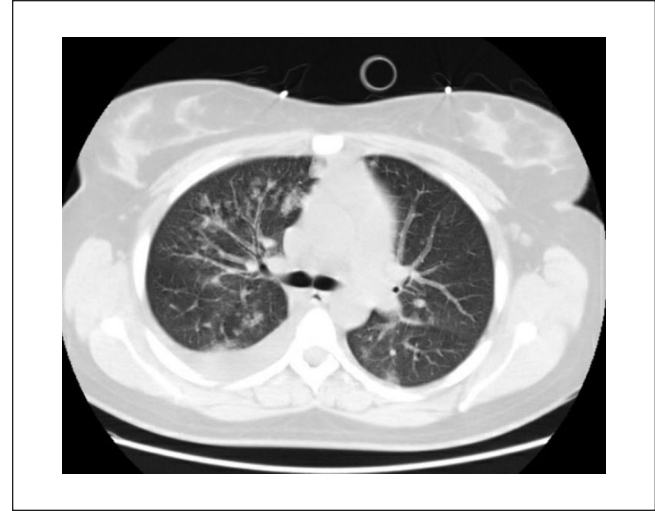


Figure 2. Computed tomography scan on day 5 of admission showing significant improvement of interstitial opacities bilaterally.

demonstrates unilateral or bilateral infiltrates, while findings on histology can include damage to the alveolar wall, inflammatory cell infiltrates, edema, hemorrhage, and necrosis.^{1,2} Because of this, there can be a lot of confusion when attempting to establish a diagnosis of lupus pneumonitis, especially during the current epidemic of COVID-19.

Treatment for lupus pneumonitis is largely empirical due to a lack of controlled studies. The mainstay of treatment is prednisone, given at 1 to 1.5 mg/kg/day.⁴ If patients fail to respond to prednisone in the first 72 hours, intravenous methylprednisolone is added at 1 g/day for 3 additional days.⁴ In patients whom steroids fail, immunosuppressive or cytotoxic agents may be used.² As mentioned before, the initiation of steroids early in the disease course is of extreme importance due to the high mortality rate of lupus pneumonitis. This is in contrast with the current treatment recommendations for COVID-19, which will be discussed below.

COVID-19

COVID-19 is a disease caused by the 2019 novel coronavirus, named severe acute respiratory syndrome coronavirus 2 (SARS-CoV2).⁶ On March 11, 2020, COVID-19 was declared a pandemic by the World Health Organization. The most common symptoms on presentation of COVID-19 include fever, dry cough, and dyspnea.^{7,8} Other symptoms that have been noted include fatigue/myalgias, sputum production, rhinorrhea, sore throat, headache, and diarrhea.^{7,8} The primary clinical features of COVID-19 are very similar to that of an acute presentation of lupus pneumonitis, which may contribute to the diagnostic uncertainty in patients presenting with these symptoms during the current pandemic.

Common laboratory values in patients presenting with COVID-19 include lymphocytopenia and elevated C-reactive protein.⁶ A lesser number of patients were found to have elevations in aspartate aminotransferase, alanine aminotransferase, creatine kinase, and D-dimer.⁶ In addition, some of the most common findings on chest imaging include ground glass opacities and bilateral patchy shadowing.^{7,8} COVID-19 has been found to have a rapidly progressive course in some patients, with one study showing the time between hospital admission and the development of ARDS to be as quickly as 2 days.⁸ The findings of lymphocytopenia and nonspecific findings on imaging prove significant overlap between lupus pneumonitis and COVID-19, as seen in this case.

Currently, there is no medical therapy known to be effective for the treatment of COVID-19; therefore, the mainstay of treatment remains supportive care.⁹ However, there are several medications in clinical trials. These include chloroquine and hydroxychloroquine, which have been used in the treatment of malaria as well as SLE and rheumatoid arthritis; lopinavir/ritonavir, which has been used in the treatment of HIV; and the antiviral medications ribavirin, remdesivir, and favipiravir.⁹ Glucocorticoids have been considered as an adjunctive therapy for COVID-19, with the rationale for their use being reduction of the inflammatory response in the lungs.⁹ However, previous studies in patients with SARS and MERS (Middle East Respiratory Syndrome) coronaviruses showed that glucocorticoids had no association with improved survival, and even delayed viral clearance and had high rates of complications.⁷⁻⁹

SLE and COVID-19

There is current controversy regarding whether patients with rheumatologic diseases such as SLE are protected from COVID-19. This controversy is primarily due to the fact that patients with SLE may be taking hydroxychloroquine at baseline. The rationale for using hydroxychloroquine in patients with COVID-19 is due to antiviral effects of the drug, including inhibiting the glycosylation of host receptors, proteolytic processing, and acidification of the endosome, all of which contribute to blocking viral entry into cells.⁹ While the drug has shown this potent antiviral activity in vitro, there have been mixed results regarding the efficacy of hydroxychloroquine for the treatment of COVID-19 in human trials.⁹⁻¹¹ In addition to this, the COVID-19 Global Rheumatology Alliance recently launched a registry to evaluate data regarding patients with rheumatologic disease who have been diagnosed with COVID-19. Initial data collected showed that of 110 patients with rheumatologic disease who had been diagnosed with COVID-19, 19 of those patients had history of SLE.¹² Last, Romão et al¹³ report 2 cases of patients with SLE who were being treated with hydroxychloroquine that subsequently developed COVID-19. In our case, we present a patient with known history of SLE who tested positive

for COVID-19 despite home treatment with hydroxychloroquine. While these cases alone are not enough to disprove claims that patients with SLE on hydroxychloroquine may have protection from COVID-19, they provide evidence that this particular patient population is certainly being affected by the novel coronavirus.

Conclusion

This case highlights a difficult clinical scenario that led to a promising improvement for the use of steroids in the treatment of our patient. Our patient presented with a possible flare up of lupus pneumonitis during the COVID-19 outbreak. The presenting symptoms between these 2 disease processes comprise significant overlap, including cough, fever, and dyspnea.^{3,7,8} In addition, lymphocytopenia has been shown to be a common laboratory finding in both pathologies.^{5,6} Due to the relatively nonspecific findings on imaging in both pathologies, we were poised with a dilemma in the face of 2 potential disease processes with the ability to rapidly progress. Due to the patient's existing condition of lupus pneumonitis, a literature search was performed to help guide management. Based on the promising cases described by Mok and Ying¹⁴ during the 2003 SARS outbreak, we decided to initiate therapy with methylprednisolone, which resulted in rapid improvement of her respiratory symptoms including a decrease in her required O₂ from 6 L to 2 L. The patient was found to be positive for COVID-19; however, she continued to improve clinically, including a significant improvement in her CT scan. She was eventually transitioned to oral prednisone, discontinued O₂, and was discharged home. Despite a lack of recommendation for the use of steroids in patients with COVID-19, our case shows promise for the use of steroids in the management of the novel coronavirus if underlying lupus pneumonitis is present.⁶⁻⁸

Declaration of Conflicting Interests

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Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent

Verbal informed consent was obtained from the patient(s) for their anonymized information.

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