To the Editor:

CASE HISTORY

A 57-year-old white woman with biopsy-proven stage I pulmonary sarcoidosis, cardiac sarcoidosis with nonischemic cardiomyopathy with an estimated ejection fraction of 37%, history of complete heart block, and ventricular tachycardia status post biventricular pacemaker with implantable cardioverter-defibrillator placement was admitted to our facility with the complaints of worsening shortness of breath and fever of 1-week duration. A week before the presentation, she tested positive for coronavirus disease 2019 (COVID-19) by detection of severe acute respiratory syndrome (SARS)-CoV-2 on polymerase chain reaction test following low-grade fevers, cough, and myalgias and was recommended to self-isolate. Her home medications included 20 mg methotrexate weekly, 40 mg subcutaneous adalimumab every 14 days, 40 mg prednisone daily, mexiletine, and amiodarone. Because of a positive COVID-19 result, methotrexate and adalimumab were held, and prednisone was continued. Vital signs on admission were a temperature of 37.8°C, heart rate 102 beats/min, blood pressure 105/75 mm Hg, respiratory rate 22 breaths/min with oxygen saturation of 92% on 2 L via nasal cannula, and body mass index of 34.3 kg/m². At baseline, patient had normal oxygen saturation >95% on room air. On physical examination, she was in minimal respiratory distress with use of accessory muscles but no cyanosis. Lung examination revealed symmetrical expansion with faint crackles bilaterally. The cardiovascular examination revealed regular rhythm and no edema. The laboratory values and trends are shown in the Table. An anteroposterior chest radiography (Fig. 1) was performed and showed mild pulmonary vascular congestion but no consolidations or infiltrates.

She was initially admitted to the medical floor, and overnight, the oxygen requirement increased from 2 to 4 L via nasal cannula. Given the leukocytosis, blood cultures were obtained, and empiric ceftriaxone was started. Patient had persistent fever with peak temperature of 39.5°C. Along with the antibiotics, oral hydroxychloroquine was initiated starting with 400 mg for 2 doses every 12 hours followed by 200 mg every 12 hours for 5 days for COVID-19 infection. Given the baseline cardiac history and use of antiarrhythmic agents, azithromycin was not used because of concern for prolonging the QT interval. Approximately 36 hours following hospital admission, patient had worsening respiratory distress with increasing oxygen

TABLE. Laboratory Data

| Test                          | Value               |
|-------------------------------|---------------------|
| White blood cell count (4.5–11) | 21.5 x 10^3/μL     |
| Red blood cell count (4.2–5.5)  | 4.37 x 10^5/μL     |
| Hemoglobin (12–16)             | 13.1 g/dL          |
| Hematocrit (37–47)             | 40.4%              |
| Platelet (150–400)             | 465 x 10^3/μL      |
| Sodium (135–145)               | 136 mEq/L          |
| Potassium (3.5–5.5)            | 4.5 mEq/L          |
| Chloride (99–109)              | 101 mEq/L          |
| Bicarbonate (20–31)            | 24 mEq/L           |
| Blood urea nitrogen (9–23)     | 13 mg/dL           |
| Creatinine (0.6–1.6)           | 0.79 mg/dL         |
| Glucose (74–106)               | 125 mg/dL          |
| Calcium (8.7–10.4)             | 9.2 mg/dL          |
| Albumin (3.2–4.8)              | 3.7 g/dL           |
| Total bilirubin (0.3–1.2)      | 0.4 mg/dL          |
| Phosphorus (2.4–5.1)           | 2.7 mg/dL          |
| Magnesium (1.3–2.7)            | 1.8 mg/dL          |
| C-reactive protein (0–0.5)     | 33.519 mg/dL       |
| D-Dimer (~<230)                | 501 ng/mL          |
| Fibrinogen (200–400)           | 576 mg/dL          |
| PTT (28–35.7)                  | 39.1 s             |
| PT (10.1–12.9)                 | 12.9 s             |
| Ferritin (10–291)              | 261.8 ng/mL        |
| Troponin I (0–0.09)            | <0.01 ng/mL        |

PT, prothrombin time; PTT, partial thromboplastin time.

FIGURE 1. Anteroposterior portable chest radiograph shows mild pulmonary vascular congestion but no consolidations or infiltrates.
requirement and the need for nonrebreather and transfer to the intensive care unit for mechanical ventilation. A subsequent chest x-ray film (Fig. 2) showed the development of bilateral pulmonary infiltrates and a slight progression in vascular congestion. Shortly following intubation, patient had hypotension necessitating vasopressors. A single dose of tocilizumab 400 mg intravenously was given at this time because of progression to severe COVID-19 infection requiring mechanical ventilation and vasopressors. Prednisone was continued as a concern for adrenal crisis related to long-term steroids. Rheumatology recommended holding methotrexate and adalimumab and continuing only the prednisone. Over the next 6 days, the vasopressors were weaned off, and she was successfully intubated and discharged home in stable condition without any oxygen requirement. Our case emphasizes the challenges in managing immunosuppressed patients with COVID-19 infection and also describes the importance of managing the immunosuppression. The most important thing is to cut down the immunosuppressive therapy carefully to treat the infection and simultaneously to avoid the flare-up of the underlying disease (Figs. 3 and 4).

DISCUSSION

The emergence of the 2019 novel coronavirus is particularly worrisome for people with sarcoidosis, not only because of these patients' already weakened immune system but also because of the symptoms of COVID-19, such as fever, cough, sore throat, and difficulty breathing, can mimic worsening of sarcoidosis. Among the general population, the case fatality rate was 2.3%, whereas it was as much higher for people with pre-existing comorbidities such as 10.5% for cardiovascular disease, 7.3% for diabetes, 6.3% for chronic respiratory disease, 6.0% for hypertension, and 5.6% for cancer. The US Centers for Disease Control and Prevention has patients with underlying comorbidities such as preexisting lung conditions under the category of high risk to acquire the infection. To the best of our knowledge, this is the first case of COVID-19 infection in a patient with sarcoidosis reported in the literature.

The exact mechanism triggering the flare-ups of sarcoidosis or interstitial lung disease (ILD) is not clear, and it could be attributed to underlying infections or idiopathic. The data on COVID-19 causing any flare-ups in patients with preexisting lung conditions are unclear at this stage, and there is a concern that it can flare up in patients with underlying fibrosis due to sarcoidosis. The mechanism of action of the immunosuppressive medications is by affecting both innate and acquired immunity or T and B cells along with the functioning of neutrophils, thus predisposing individuals to a greater risk of infections.

Our patient was chronically immunosuppressed and has been on maintenance methotrexate, adalimumab, and a tapering dose of prednisone. The inflammation is prominent and is associated with a myriad of adverse outcomes such as acute lung injury and acute respiratory distress syndrome in patients with COVID-19. Pulmonary histology from patients revealed inflammation and diffuse alveolar damage. Corticosteroids suppress lung inflammation but also inhibit immune responses and pathogen clearance. Studies have shown that steroids prolonged viral shedding in patients infected with SARS and Middle East respiratory syndrome. Therefore, extreme caution has to be exercised prior to prescribing...
steroids, as steroids are the cornerstone in patients with a history of chronic obstructive pulmonary disease or asthma or ILD.6

The treatment for the COVID-19 is symptomatic, including self-isolation to oxygen supplementation, mechanical ventilation, extracorporeal membrane oxygenation, use of hydroxychloroquine, azithromycin, tocilizumab, remdesivir, and convalescent plasma.6,7 Additionally, drugs such as tocilizumab, a recombinant humanized anti-human interleukin 6 (IL-6) receptor monoclonal antibody, could be of great help in patients with severe COVID-19. This is due to the drug’s mechanism of targeting the IL-6 pathway by binding to the IL-6 receptor and continuing the prednisone and symptomatic treatment. Recently, on April 29, 2020, Mikuls et al.8 published American College of Rheumatology guidelines for the management of rheumatologic diseases during the COVID-19 pandemic, and it has been suggested that glucocorticoids should not be abruptly stopped, regardless of exposure or infection status (high level of task force consensus). Regardless of COVID-19 severity, antimarial therapies (hydroxychloroquine/chloroquine) may be continued, but sulfasalazine, methotrexate, leflunomide, immunosuppressants, non-IL-6 biologics, and JAK inhibitors should be stopped or held (moderate to high level of task force consensus).8 Methotrexate, in particular, can cause a pneumonitis and accelerate ILD; thus, it was particularly important to hold it in this patient with COVID-19 pneumonia and underlying stage I pulmonary sarcoidosis who was on relatively high-dose methotrexate.

Despite her underlying cardiac and pulmonary comorbidities requiring chronic immunosuppressive therapy, she recovered from her illness and was discharged home. Although prednisone has been reported to cause immunosuppression and may prolong the duration of viral shedding, because of its anti-inflammatory properties and combination with the tocilizumab, it may have been helpful in suppressing the systemic inflammation already present with the sarcoidosis and exacerbated with SARS-CoV-2, thereby allowing recovery to ensue for this patient. Because our patient was simultaneously treated with ceftriaxone empirically for community-acquired pneumonia, it is a possibility that her clinical improvement was due to treatment of a superimposed bacterial pneumonia. However, we favor that our patient’s respiratory failure and critical illness were secondary to COVID-19 pneumonia alone due to her positive SARS-CoV-2 polymerase chain reaction testing prior to admission, typical COVID-19 presenting symptoms, short duration between hospital admission and respiratory decompensation, negative bronchoalveolar lavage at the time of intubation, and negative blood cultures. A CT scan of the chest was not performed in this case. Both COVID-19 pneumonia and non-COVID-19 pneumonias most often demonstrate ground-glass opacities and/or consolidations on chest CT, and chest CT has a low specificity of 25% for COVID-19 pneumonia,9 making it unlikely to have changed management in this case.

As the innate immune system is responsible for host tissue damage,9 whether the coronavirus infection will cause severe to critical illness in the immunosuppressed patients needs to be investigated. As the mortality rate is more than 50% during the ILD flare-ups, it is of utmost importance to diagnose these patients earlier in the disease process and treat them appropriately.7,10

CONCLUSIONS

Infection with SARS-CoV-2 can vary widely from an asymptomatic course to mild, severe, or critical illness. The overall morbidity and mortality are much higher in patients with known comorbidities such as coronary artery disease, diabetes, hypertension, cancer, and autoimmune diseases. For patients with comorbidities requiring long-term immunosuppressive therapy, such as those with autoimmune diseases, a multidisciplinary approach is of utmost importance. Further studies are needed to identify the best management options for patients on chronic immunosuppressive therapy.

KEY POINTS

• Lower threshold to admit patients with underlying history of immunosuppression.
• Cardiac sarcoid is a leading cause of death in sarcoidosis, and the frequency of cardiac relapse is high and may be life-threatening.

FIGURE 4. C-reactive protein trend during the hospitalization. Color online-figure is available at http://www.jclinrheum.com.
Managing cardiac sarcoidosis with severe COVID-19 infection requires multidisciplinary approach, given no robust evidence.

Prednisone should be continued to prevent adrenal crisis in patients on long-term steroids.

Regardless of COVID-19 severity, hydroxychloroquine may be continued, but sulfasalazine, methotrexate, leflunomide, immunosuppressants, non-IL-6 biologics, and JAK inhibitors should be stopped.

Our institution does not require ethical approval for reporting individual cases or case series. Verbal informed consent was obtained from the patient for her anonymized information to be published in this article. The authors declare no conflict of interest.

Author Contributions: S.A.P. and V.M.M. made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data. S.A.P., V.M.M., A.M., A.V., R.E., and S.J.G. were involved in drafting the manuscript or revising it critically for important intellectual content. S.A.P., V.M.M., A.M., A.V., R.E., and S.J.G. gave final approval of the version to be published. Each author has participated sufficiently in the work to take public responsibility for appropriate portions of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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