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Case report

COVID-19 in a patient with a flare of systemic lupus erythematosus: A rare case-report

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ABSTRACT

This is a rare case-report of a young female with systemic lupus erythematosus and end-stage kidney disease (on maintenance hemodialysis) who was admitted to our intensive care unit due to life-threatening COVID-19. The patient was diagnosed with a flare of lupus; while being on maintenance hydroxychloroquine therapy. However, after the administration of steroids she made an uneventful recovery and was discharged home. In this report, the diagnostic dilemmas and the therapeutic challenges due to the overlapping clinical, imaging, and laboratory findings between lupus and COVID-19 pneumonitis are outlined. In conclusion, patients with lupus may be affected by COVID-19 despite the administration of hydroxychloroquine. The administration of steroids may have a beneficial effect on mitigating both the flare of SLE and the COVID-19 associated hyperinflammation.

1. Introduction

The novel coronavirus SARS-CoV-2 disease (COVID-19) emerged in Wuhan, the capital of Hubei province, in China, and progressively spread worldwide [1–3]. A minority of patients can develop fulminant disease, which is characterized by acute respiratory distress syndrome (ARDS), sepsis, thromboembolic disease, and multi-system organ failure [4,5]. Old age and underlying disorders such as arterial hypertension, diabetes mellitus, end-stage kidney disease (ESKD), and compromised immune status are risk factors affecting the morbidity and the mortality of COVID-19 patients [6–8]. The incidence of COVID-19 in patients with autoimmune disorders was not extensively studied. Also, great controversy exists about the potential role of hydroxychloroquine as protective therapy against COVID-19 in patients with systemic lupus erythematosus (SLE). Hydroxychloroquine was used in COVID-19 therapy due to its *in vitro* antiviral effects such as inhibition of the glycosylation of host receptors, and endosome acidification, amongst others, preventing likely the viral entry into the host cells (*in vivo*). However, the results in human trials were indeed controversial or even discouraging [9–11]. This report outlines diagnostic and treatment challenges in a young female COVID-19 patient with a flare of SLE.

2. Case presentation

A 28 year old female with a past medical history of SLE was admitted to the emergency department due to recent onset fever (38.8 °C), persistent cough, fatigue and progressive dyspnea. Also, she had ESKD due to lupus nephritis Grade VI, and being on maintenance hemodialysis via an arteriovenous fistula for the last three years. The patient's medications integrated hydroxychloroquine and mycophenolic acid as part of her SLE home management. Her mother revealed that she had protected (wearing a surgical mask) contact (one week ago) with one of her sisters who had just recovered from a flu-like illness. Since the endemic wave of COVID-19 had already affected Riyadh, the capital city of Saudi Arabia, we were alerted for a possible SARS-CoV-2 infection; hence, nasopharyngeal swabs were derived urgently and sent for testing.

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Moreover, we contacted the family physician requesting that her sister should be tested according to our Ministry of Health recommendations for COVID-19. Consequently, the sister was also tested positive for COVID-19 but was asymptomatic at that time. Hence, in our patient, the time period from symptoms onset to emergency department admission was approximately nine days.

On physical examination decreased breath sounds and crepitations at the lung bases were evident. Her saturation of peripheral oxygen (SpO_2) was 88%, on room air, and she had minor respiratory distress. She received 5 L of oxygen via a nasal cannula. Thereafter, the patient desaturated further (SpO_2: 75%) and developed a picture of septic shock. Therefore, she was intubated and resuscitated by the intravenous administration of 500 ml of normal saline and low dose of noradrenaline to maintain a mean arterial pressure of 70 mm Hg. Electrocardiogram, cardiac enzymes, and echocardiography were normal. Laboratory findings were normal apart from lymphocytopenia (0.59 × 10^9/l, normal: 1.1–3.2 × 10^9/l), and increased C-reactive protein (354 mg/liter, normal: 0–7 mg/l), d-dimer (1.9 mcg/ml, normal: 0 to 0.5 mcg/ml), lactate dehydrogenase (737 units/l, normal: 100–190 units/l), and ferritin (1.126 ng/ml, normal: 23–336 ng/ml). Her blood urea nitrogen was 7.9 mmol/l (normal: 2.5–6.4 mmol/l) and creatinine 239 μmol/l (normal: 71–115 μmol/l). Emergency contrast chest computed tomography (CT) scan excluded pulmonary embolism but confirmed bilateral ground-glass opacities that were distributed in both the upper and lower lobes of the lung (Fig. 1). Subsequently, nasopharyngeal swabs confirmed COVID-19 by Real-Time-Polymerase-Chain-Reaction (RT-PCR) assays using QuantiNova Probe RT-PCR kit (Qiagen) in a Light-Cycler 480 real-time PCR system (Roche, Basel, Switzerland) [12–14].

The patient was admitted to one of the 100 isolation chambers designated for COVID-19 supportive care within our 200-bed polyvalent intensive care unit (ICU). The patient underwent a full diagnostic work-up for other viral and bacterial infections. Also, the evaluation for a flare of SLE was initiated accordingly. The patient did not have any cutaneous manifestations of SLE or oral ulcers; furthermore, morning stiffness, and synovitis could not be properly assessed as the patient was intubated at that time. Laboratory tests showed elevated levels of anti-dsDNA at 22 IU/ml (normal values: <10 IU/mL) and decreased serum complement levels C3/C4 at 64 and 6 mg/dl, respectively [normal values: C3 (88–201 mg/dl) and C4 (10–40 mg/dl)]. No anti-cardiolipin antibodies, anti-β2GP1 antibodies, lupus anticoagulant or thrombocytopenia were detected. The diagnostic dilemma between rapidly evolving lupus pneumonitis and COVID-19 pneumonia emerged. Cultures were derived from all sites to investigate for any bacterial infections as the patient remained febrile. Bedside sonographic examination of the lower limbs excluded deep vein thrombosis. Empiric therapy for COVID-19 with lopinavir/ritonavir and ribavirin, piperacillin/tazobactam, as well as prophylactic anticoagulation along with sessions of hemodialysis every 48 hours, and supportive ICU care was administered as per hospital protocol [15]. Due to the fact that her fistula was malfunctioning a double lumen central line was inserted for hemodialysis (Fig. 2). Approximately three days post-ICU admission, the ratio of partial arterial pressure of oxygen to fractional inspired concentration of oxygen (SpO_2/FiO_2) was 150 despite the application of ARDS-net and prone positioning ventilation (positive end-expiratory pressure of 10 cm H_20). On day-3, we decided the initiation of steroid treatment based on the pertinent clinical and laboratory data. After rheumatology consultation, we administered pulse methylprednisolone therapy (1 g/day intravenously) for three days (the patient's body weight was 60 kg). On day-4 post-ICU admission, the SpO_2/FiO_2 ratio increased to 300, and vasopressors were discontinued. On day-6, the patient was successfully extubated, and was placed on high flow nasal cannula (flow: 60 L/min, and FiO_2 of 40%) maintaining SpO_2 level over 96%. Notably, laboratory parameters improved as lymphocytes increased from 0.59 to 0.88 × 10^9/l, and inflammatory biomarkers decreased: [C-reactive protein: from 354 to 37 mg/l; d-dimer: from 1.9 to 1 mcg/ml; lactate dehydrogenase: from 737 to 301 units/liter; and ferritin: from 1.126 to 381 ng/ml]. On day-8, the patient was placed on 2 L of oxygen via a nasal cannula without showing any respiratory distress. The results of all cultures for bacterial infections were negative. We continued her usual maintenance hemodialysis regime and steroid therapy. Oxygen supportive care was discontinued on day-10, and the methylprednisolone was tapered down to 60 mg per day (1mg/kg/day). RT-PCR test for COVID-19 and repeated microbiology tests were negative on day-17. The patient refused any follow-up testing, thus she was discharged to home isolation on day-19, on maintenance oral steroid therapy, and she is thereafter followed-up by her family physician.

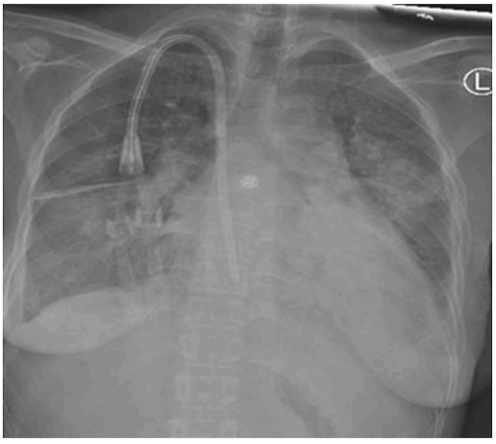

Fig. 2. Portable chest X-ray depicting bilateral interstitial infiltrates (the venous catheter is a double-lumen central line, which was inserted for hemodialysis as the patient's fistula was malfunctioning at that time).

3. Discussion

In this case-report, a puzzling clinical scenario is encountered. Our patient had COVID-19 pneumonia and a flare of SLE. Her presenting

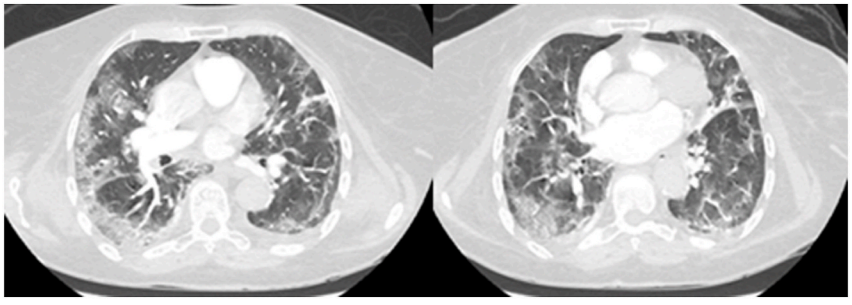

Fig. 1. Emergency contrast chest computed tomography scans revealing peripheral bilateral patchy ground-glass opacities with consolidations. Pulmonary embolism was excluded in our lupus patient with COVID-19.

symptoms of fever, cough, dyspnea, hypoxia, and lung crepitations can be observed both in lupus and COVID-19 pneumonitis [2–8,16–19]. Moreover, lymhocytopenia can be a hallmark feature in both disorders [4–6,20]. Apart from lymphocytopenia, other hematologic abnormalities including hemolytic anemia, leukopenia, and thrombocytopenia are included in the 2019 classification criteria for SLE by the American College of Rheumatology [20]. However, the aforementioned laboratory findings were not evident in our patient. Also, lupus pneumonitis could exhibit non-specific radiography and histology findings. Chest X-rays could demonstrate unilateral or bilateral infiltrates; while chest CT scans could depict ground-glass opacities. Findings on histology include alveolar wall damage, inflammatory cell infiltrates, edema, hemorrhage and necrosis [16–19]. There is a significant overlap of findings between lupus and COVID-19 pneumonitis, and thus confusion may arise when trying to establish a diagnosis of lupus pneumonitis during the COVID-19 pandemic [16–19,21,22].

SLE patients with serious viral pneumonitis can be treated by the administration of steroids [23,24]. However, our COVID-19 patient with SLE had life-threatening features such as rapidly evolving septic shock and ARDS [2–8], which were not documented in previous reports [24]. ESKD might have at least partially contributed to the severity of the clinical picture, although not affecting unfavorably the outcome in our case [2–8]. Moreover, the standardized hemodialysis sessions along with the administration of other therapies, and the supportive ICU care may also contributed to the improvement of the patient's oxygenation. Antiviral agents such as remdesivir along with immunomodulatory therapies such as convalescent plasma transfusions, the new monoclonal antibody against interleukin-6 (tocilizumab), and plasma exchange showed promise in the treatment of COVID-19 but remain largely empiric [25–29].

The administration of steroids was not recommended in COVID-19, until recently, when the results of the beneficial role of low-dose dexamethasone therapy were reported in the RECOVERY trial [30]. In contrast, other recently published data showed no effect on 28-day mortality in critically ill COVID-19 patients after the administration of methylprednisolone (METCOVID trial), although patients over 60 years had a lower mortality in a subgroup analysis [31]. In our study, steroids were administered due to the flare of lupus in a young female patient. We are uncertain whether methylprednisolone mitigated as well the cytokine storm related to COVID-19 [27–29,32,33]; however, given the severity of our patient's clinical picture it might have helped. The putative beneficial effect of steroids on viral pneumonitis was previously advocated in critically ill patients with Middle East Respiratory Syndrome [34]. This remains to be further studied in critically ill patients with COVID-19 along with the potential sequela of the administration of steroid therapy such as delaying of the viral clearance, and increasing the rate of secondary bacterial infections [6–8].

The most common signs and symptoms of lupus pneumonitis are fever, cough with lung crepitations and ensuing hypoxemia, which were also observed in our patient with SLE. Several pulmonary manifestations of SLE such as pleural and lung parenchymal involvement, pulmonary hypertension, diffuse alveolar hemorrhage, and thromboembolic disease, amongst others, are well documented [16–20]. However, lupus pneumonitis occurs only in a minority (1–4%) of SLE patients and carries a poor prognosis; while its therapy is still empiric. The basis of treatment is the administration of prednisone (1–1.5 mg/kg/day), and if there is no response, intravenous methylprednisolone (1g/day) can be added for three days [16–20]. The administration of steroid therapy, early in the course of lupus pneumonitis, is important due to its high mortality rate. If steroid therapy fails, other immunosuppressive or cytotoxic agents can be used. Fortunately, our patient responded favorably to the administration of steroid therapy.

Notably, this case-report underlines another trending controversy: the putative protective action of hydroxychloroquine in COVID-19. Recent data from the COVID-19 Global Rheumatology Alliance Registry recorded nineteen patients suffering from SLE out of the one hundred and ten rheumatologic patients who were diagnosed with COVID-19 [35]. Other studies provided evidence that the administration of hydroxychloroquine was not protective against COVID-19, which is in accordance with our current observations [36].

This case-report, albeit its many limitations that prevent its generalizability, carries important messages. Patients with SLE may be affected by COVID-19 despite the administration of hydroxychloroquine. The diagnostic dilemmas and the therapeutic challenges should be carefully processed due to the overlapping clinical, imaging, and laboratory findings between lupus and COVID-19 pneumonitis. In conclusion, the administration of steroids may have a beneficial effect on suppressing both the flare of SLE and the COVID-19 associated hyperinflammation. Further large prospective studies are required to confirm or refute the present findings.

CRediT authorship contribution statement

Abdulrahman Alharthy: Conceptualization, Investigation, Validation, Writing - original draft. **Fahad Faqihi:** Investigation, Validation, Writing - original draft. **Nasir Nasim:** Validation, Writing - original draft. **Alfateh Noor:** Investigation, Validation, Data Analysis. **Saima Akhtar:** Validation, Data Analysis. **Ahmed Balshi:** Investigation, Validation, Data Analysis, Writing - original draft. **Abdullah Balhamar:** Validation, Writing - original draft. **Saleh A. Alqahtani:** Supervision, review & editing, and revising the final draft. **Ziad A. Memish:** Validation, Supervision, review & editing the final draft. **Dimitrios Karakitsos:** Conceptualization, review & editing, and revising the final draft.

Declaration of competing interest

None.

Abbreviations

SARS-CoV-2 disease	COVID-19
ICU	intensive care unit
RT-PCR	Real-Time-Polymerase-Chain-Reaction
CT	computed tomography
SLE	systemic lupus erythematosus
ESKD	end-stage kidney disease
ARDS	acute respiratory distress syndrome
SpO_2/FiO_2 ratio	partial arterial pressure of oxygen to fractional inspired concentration of oxygen ratio

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Ethical approval

The study was approved by the Institutional Review Board of King Saud Medical City, Riyadh, Kingdom of Saudi Arabia [H-01-R-053, IORG0010374, H1RI-7-2020]. Written informed consent was obtained from the patient.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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