

## A Lupus Flare Case, After Infection With COVID-19

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### ABSTRACT

**Introduction:** Lupus is a systemic autoimmune disease with multi organ involvement, that develops a variety of clinical manifestations from dermatological ones to severe organ damage. Covid 19 is an infection with high mortality and morbidity, caused by the novel severe acute respiratory syndrome (SARS) coronavirus 2 (CoV2). There are hypotheses on a burst of clinical manifestations of Systemic Lupus Erythematosus (SLE) after Covid 19, based on different literature reports. Here we present a clinical case of SLE with organ involvement, which aggravated after infection with SARS Cov2.

**Clinical case:** A 30 year old young woman presented with aggravation of her musculoskeletal symptoms after infection with Covid 19. Before the coronavirus infection, she had joint pain, fatigue and subsequently developed systemic multiorgan involvement like lupus nephritis, pulmonary and hematological involvement. The patient gets diagnosed with SLE and begins treatment with Methylprednisolone 1 gram/day for three days, followed by ACE I (Ramipril 5 mg 1 tab/day), Mycophenolate 3 gram/day, Plaquenil 200 mg/day, Prednisone 1mg/kg body weight, Calcium, Vitamin D, PPI.

**Conclusion:** With this clinical case we underline a hypothesis of a burst of clinical manifestations of autoimmune diseases, SLE in this case, probably because of a high titer of antibody production after infection with Covid 19.

**Keywords:** Systemic Lupus Erythematosus, SLEDAI, FLARE, Covid-19

### Introduction

SARS-CoV-2 is the newest coronavirus, linked to causing a series of atypical respiratory diseases in Hubei, province of Wuhan, China in December 2019. The disease caused by SARS-CoV-2 was named COVID-19 and it was declared a pandemic from WHO in March 2020 (Pollard *et al.*, 2020). The antiviral immune response, though very important for protecting against SARS-COV-2 infection, comprises of a cytokine storm which can be uncontrolled and can cause severe organ damage with high mortality (Spihlman *et al.*, 2020). Systemic lupus erythematosus (SLE) is a chronic inflammatory disease, that affects more women than men, and is one of the main causes of death in young women. Viral infections serve as triggers to an excessive immune response, leading to cytokine overproduction in some genetically predisposed patients (Spihlman *et al.*, 2020; Caso *et al.*, 2020; Doaty *et al.*, 2016; Ramos-Casals, 2008). This is our experience with a clinical case, where a patient suffering from SLE, gets infected

with SARS-COV-2 and develops a severe disease.

## Case Presentation

A 30 year old female patient comes to the emergency room referring joint pain and swelling, intermittent fever, difficulty breathing, fatigue and diffuse alopecia. The patient has been on glucocorticoids and antibiotics on the last two weeks.

On physical examination, she was alert and oriented x4. On auscultation, bilateral diminished breath sounds and tachycardic. Her vitals show temperature of 38.5 degree Celsius, BP 160/100 mmHg and a heart rate of 115/min. On palpation she had joint pain with signs of synovitis in her knees and metacarpophalangeal joints. There is edema in her palpebrae and pitting edema in the extremities.

The anamnesis involves a medical history of 3 months referring intermittent joint pain and swelling, and low grade temperature of 37.5 degree Celsius, for which she has received symptomatic treatment with Non Steroidal Anti inflammatory Drugs (NSAIDs) and Glucocorticoids. The patient did not do further diagnostic examinations. Four weeks ago, she was diagnosed with Covid-19, with symptoms of a fever, dry cough, myalgia and arthralgia. Her PCR test showed a positive SARS-COV2 result and she was treated by her family doctor with Azithromycin 500 mg/day, Vitamin C 1 gram/day and antipyretics. She clinically improved after the treatment.

The patient is hospitalized and undergoes further examinations. Her CBC shows: E:  $3.5 \times 10^6$ /uL, L  $3 \times 10^3$  K/uL, PLT  $105 \times 10^3$  K/uL, Hgb 10.7 g/dL. In the biochemistry panel we notice a preserved renal function, but with low levels of albumin 2.2 g/dL. The total protein in serum is 5.4 g/dL and lipids show a LDL Chol of 199 mg/dL, TG 282 mg/dL, HDL 44 mg/dL, Chol 280 mg/dL. The urine analysis demonstrates a protein level of 150 mg, erythrocyte 200 uL and leukocyte 150 uL. The antibody test is performed on the patient's blood and detected a high titer of IgG antibody to SARS-CoV2 1560 (>1.1).

The heart ultrasound demonstrates pericardial effusion, with a normal heart structure and function.

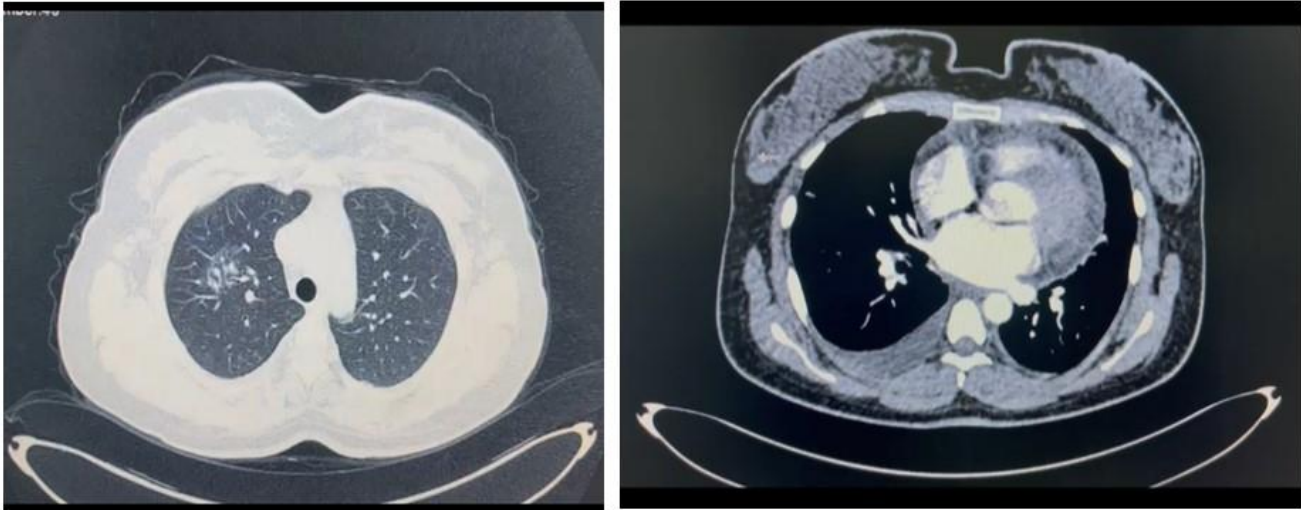
The pulmonary CT scan showed inflammatory fibrotic lesions in the right superior lobe, with minimal bilateral pleural fluid (Fig. 1). Other structures were otherwise normal.

The bronchoscopy was normal and the bronchoalveolar lavage for Koch's bacillus was negative.

Patient was evaluated by rheumatologist and underwent various immunological laboratory examinations. The immunological panel shows: ANA 1:560, PCR 15 (<5), ENA positive (Anti ds DNA+,

Nucleosome+, Anti SM+), FR negative, Anti CCP negative, P, C-Anca negative, C3 37 (low), C4 (low) and 24 hour-proteinuria 3529 mg.

All these examinations tell us that we are dealing with a diagnosis such as SLE, with a high activity of SLEDAI 33, with multiorgan involvement.



**Figure 1:** inflammatory fibrotic lesions in the right superior lobe, with minimal bilateral pleural fluid.

Based on the patient medical history, we can presume that she had a history of complaints regarding a rheumatological nature, but that was manifested heavily after getting infected with SARS-COV-2, involving multiple organs, such as polyserositis, lupus nephritis, pulmonary and hematological involvement. She was immediately started treatment with Methylprednisolone 1 gm/day for 3 days, ACE-I (Ramipril 5 mg 1tab/day), MMF 3gr/day, Plaquenil 200 mg/day, Calcium, Vitamin D3, PPI. A renal biopsy was required, but that was refused by the patient. She continued treatment with Prednisone 1mg/kg of body weight, MMF and Plaquenil until her inflammatory tests and proteinuria were stabilized.

After 3 weeks of hospitalization, the patient is discharged with a reduced disease activity of SLEDAI 12. Tapering of prednisone dose was made during a period of 6 months, until a dose of 7.5 mg/day was reached. Treatment with MM 3 gr/day, Plaquenil 200 mg/day, Calcium, Vitamin D3, Ramipril and PPI was continued. One year later, the patient has achieved remission of the disease, with laboratory follow up showing ANA 1:320, lower titer of Anti ds DNA, normal C3 and low C4.

## Discussion

Lupus is a chronic autoimmune inflammatory disease, with systemic organ involvement. Though the etiology is not clearly known, genetic and environmental causes are thought to play a part. Viral infections have been discussed to serve as a precipitating factor for the disease. T lymphocyte

autoactivation plays a key pathogenic role, producing proinflammatory cytokines and activating B lymphocytes, this leads to antibody production that attack cells and tissue (Illescas-Montes *et al.*, 2019). Since 1971, Epstein Barr virus has been discussed to be one of the causative viruses, with other viruses being mentioned in the literature, such as CMV, Parvovirus B19, HERV (human endogenous retroviruses), each one acting with different immunological mechanisms (Quaglia *et al.*, 2021; James and Robertson, 2012; James *et al.*, 2001). Several studies have confirmed that in response to these viruses, SLE patients produce higher levels of antibodies and PCR (polymerase chain reaction) products, as compared to controls. This can contribute in many cases in causing a flare of the disease activity (James *et al.*, 2001; Nelson *et al.*, 2014; Rigante *et al.*, 2014).

Regarding the same theory, it is thought that Covid-19 can cause an exacerbation of autoimmune diseases and antibody overproduction. Different hypothesis show that this can happen in patients that are genetically predisposed to develop autoimmune disorders, but further studies will be needed to confirm these assumptions (Gracia-Ramos and Saavedra-Salinas, 2021; Caso *et al.*, 2020). Specialists suppose that SARS-CoV-2 can produce a self-tolerance disruption and an autoimmune response through cross reactivity with host cells (Liu *et al.*, 2021). It is also noted a production of antibodies like ANA, antiphospholipid antibody, ANCA, anti CCP, Ro/SSA; which are thought to play a part in SLE exacerbation. (Gazzaruso *et al.*, 2020; Gracia-Ramos *et al.*, 2021; Zamani *et al.*, 2021)

In literature, this is not the only case describing this association (Khalid *et al.*, 2021; Alharthy *et al.*, 2020). This can explain the SLE disease aggravation after infection with Covid-19, as in our clinical case, along with severe organ involvement. Clinical condition monitoring, but also antibody titer, during and after Covid-19 infection is needed in patients that are predisposed to suffer from autoimmune disorders or already diagnosed with an autoimmune disease, to further prevent flares with a high activity of the disease.

## Conclusion

There are clinical cases and small studies in literature about the effects of Covid-19 and SLE first time clinical manifestations (Ahmed *et al.*, 2021; Raghavan *et al.*, 2019; Zamani *et al.*, 2021), but there isn't still a definite conclusion. This will require major studies, with a greater number of patients. Nevertheless, clinicians should be aware of this phenomenon, which is becoming more and more evident after infection with Covid-19. An evaluation of the immunological disorder is recommended in these cases, and its role in the aggravation of an autoimmune disease (Taeschler *et al.*, 2022; Sacchi *et al.*, 2021).

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