CASE REPORT

Newly Diagnosed Systemic Lupus Erythematosus in a COVID-19 Positive Patient: A Case Report

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ABSTRACT

Systemic lupus erythematosus (SLE) is an autoimmune disease with a wide range of clinical presentations. Its early manifestations may not be specific thus proper investigations and diagnosis may be hindered. Coronavirus disease (COVID-19), primarily an infectious respiratory illness, is caused by the novel coronavirus SARS-CoV-2 that was recently discovered in 2019. We report a case of a newly diagnosed SLE in a COVID-19 patient who presented with worsening fluid retention and renal function.
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INTRODUCTION

Coronavirus disease 2019 (COVID-19) – caused by severe acute respiratory syndrome coronavirus (SARS-CoV-2) – was declared a pandemic in early 2020 by the World Health Organization (WHO). As of 26th April 2022, more than 500 million confirmed cases were reported with the death toll of up to 6.2 million worldwide. In Malaysia, a total of 4.4 million people were infected by COVID-19 with 35,507 deaths reported. Among the general population, the elderly and people with certain underlying medical conditions are more prone to severe infection. The risk is also higher in immunocompromised individuals including autoimmune diseases such as systemic lupus erythematosus (SLE).

SLE is a chronic autoimmune disorder with female preponderance and is more common among Africans, Latin Americans, and Asians. It has a wide spectrum of severity and disease course. The variable clinical presentations among patients may halt a timely diagnosis and proper management of SLE. Several articles have reported on the possible associations between COVID-19 and SLE. We aim to highlight the impact of COVID-19 on a newly diagnosed SLE with possible lupus nephritis in this case report.

CASE REPORT

A 56-year-old Malay lady with underlying diabetes mellitus type 2, hypertension, and dyslipidaemia was admitted to our centre due to generalised oedema associated with lethargy and orthopnoea, and concomitant COVID-19 infection.

She had history of fever with cough for two days, and rapid antigen self-test was positive for COVID-19. She went to a COVID-19 Assessment Centre the next day and was also noted to have bilateral lower limb swelling associated with lethargy and orthopnoea for the past one month. She frequently missed her medications and her highest blood pressure recorded at home was 200/100mmHg. She was hence referred to our centre (at that time a dedicated COVID-19 hospital) for further management.

Upon further history taking, patient was informed that her creatinine level showed an increasing trend during a clinic follow up, six week prior to this admission. An appointment date was given to further investigate the cause of kidney injury by the clinic. However, due a to long waiting time for the appointment (it was during the Delta wave of COVID-19) and worsening of the lower limb swelling and lethargy, she went to a private health care centre three weeks later. At that time, her creatinine level had increased to 177 mmol/L. Ultrasonography (USG) of the kidneys, ureters and bladder (KUB) done at the private health care centre as an outpatient two

weeks after that showed normal KUB with no obstructive uropathy or parenchymal disease. However, massive ascites was noted.

On examination, the patient was mildly tachypnoeic with generalised oedema and ascites. She was afebrile with BP of 141/60mmHg, pulse rate of 87 beats per minute, respiratory rate of 20 breaths per minute, and SpO2 under room air of 95%. Chest radiograph on admission showed blunted right costophrenic angle and minimal right pleural effusion (Fig. 1). Initial blood investigations revealed normochromic normocytic anaemia, elevated serum urea, creatinine and ferritin levels, and non-reactive infective screening (Table I).

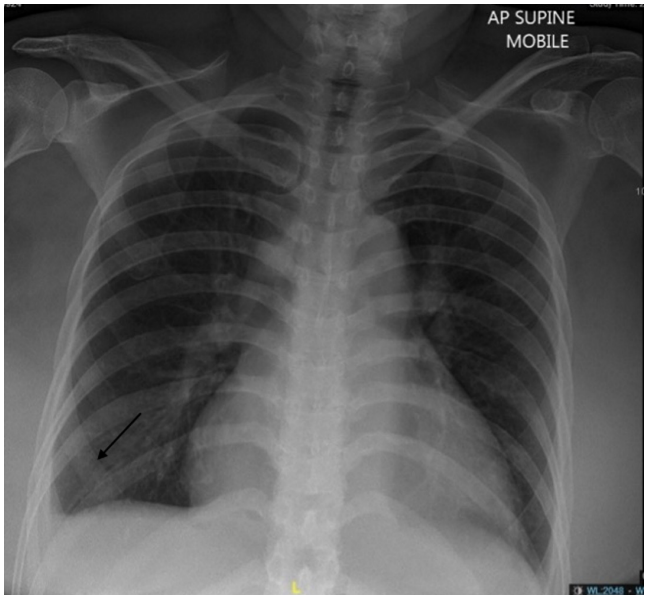

Figure 1: Chest radiograph taken on day of admission showed cardiomegaly with blunted right costophrenic angle (black arrow) and minimal right pleural effusion.

A diagnosis of 'COVID Category 2 with fluid overload secondary to hypertensive cardiomyopathy in failure, acute kidney injury on chronic kidney disease, generalised anasarca due to hypoalbuminaemia and coagulopathy' was made. However, her diagnosis was revised to 'COVID-19 Category 4' the next day following desaturation under room air (SpO2 93%) during transfusion of 1-pint packed cells.

The patient was intubated a few days later due to type 1 respiratory failure and deteriorating level of consciousness with Glasgow Coma Scale (GCS) assessment at E3V5M6 and worsening SpO2. A repeat chest radiography showed dense consolidation of the middle and lower zones of both sides of the lungs (Fig. 2). The diagnosis was revised to 'COVID-19 Category 5 with possible nephrotic syndrome'. She was started on intravenous (IV) albumin infusion and glucocorticoids and investigated for nephrotic syndrome. She was extubated four days later and was stable until coffee

Table I: Summary of patient's blood results

Indices	Baseline	On admission	Peak/nadir values
Haemoglobin (g/dL)		6.3	6.8
White blood cell (x10^9/L)		6.56	13.6
Platelet (x10^9/L)		236	140
Absolute lymphocyte (x10^9/L)		0.93	0.2
Blood urea nitrogen (mmol/L)		20	52.1
Creatinine (umol/L)	98	176	412
Prothrombin time (sec)		14.30	
APTT (sec)		114.9	
INR		1.08	
C-reactive protein (mg/dL)		5.6	
Ferritin (ug/L)		363	
C3 (g/L)			0.79
C4 (g/L)			0.29
Antinuclear antibody *(Indirect immunofluorescent)*			Positive (1:320) Homogenous pattern
Anti-double stranded DNA *(Indirect immunofluorescent)*			Positive
Protein/Creatinine Index			Urine protein 2.36 g/L Creatinine urine 4825 umol/L PCI 0.489 (normal: 0.00 – 0.020)

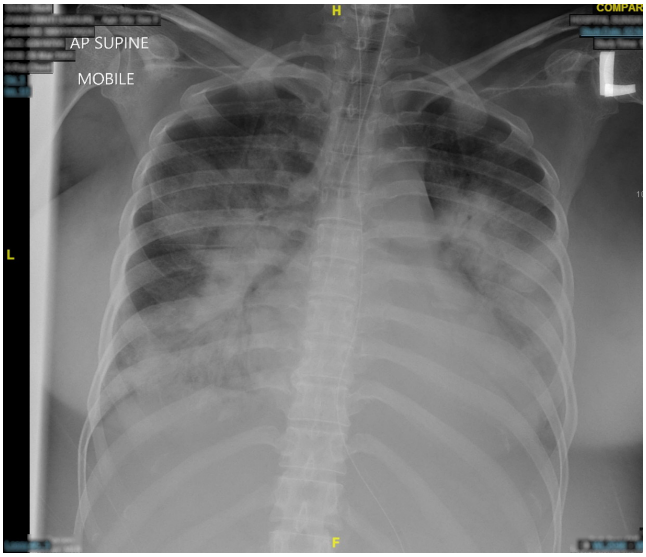

Figure 2: Chest radiograph taken on day of first intubation. Dense consolidations could be seen in middle and lower zones of bilateral lungs, relatively sparing bilateral upper zone.

ground aspirate was noted during the suction of Ryle's tube. IV Pantoprazole was started, and she was referred to the surgical team.

Her serum urea and creatinine levels showed a worsening trend, and her urine protein creatinine index was high (0.489). In view of rapid deterioration of kidney function, the nephrology team was consulted. Lupus nephritis was suspected, and blood samples were sent for connective tissue disease screening. Antinuclear

antibody test was positive (homogenous pattern, titre 1:320), anti-dsDNA was detected, and serum C3 was low (Table 1). Her diagnosis was revised to 'SLE with possible lupus nephritis'. Renal biopsy was planned to confirm the diagnosis once her condition has stabilised, and she no longer has active COVID-19 infection.

The patient was dialysed three days later for worsening renal function and reintubated on the same day due to respiratory distress. She managed to be extubated on day 21 of hospitalisation and was covered for hospital-acquired pneumonia with IV Colistin. High-resolution computed tomography (HRCT) of lungs on the day of extubation showed bilateral perihilar consolidation (Fig. 3). Unfortunately, despite aggressive care and management, the patient passed away the following day due to severe nosocomial pneumonia and fluid overload.

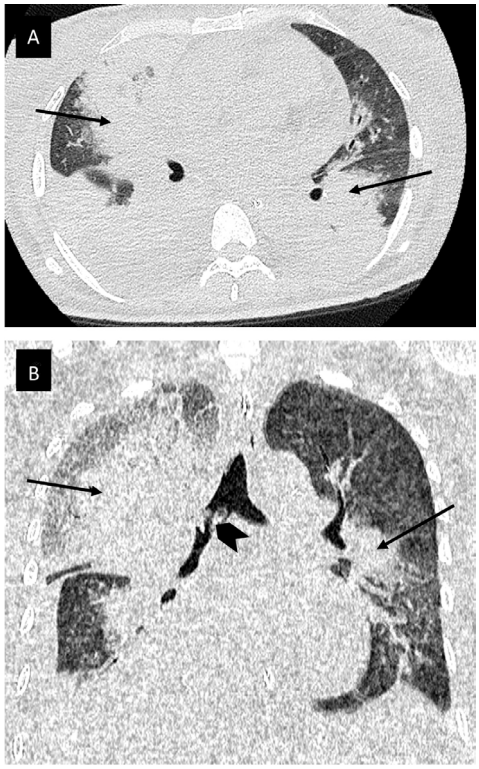

Figure 3: HRCT of thorax in lung window in axial view (A) and coronal view (B) showed bilateral perihilar consolidation (black arrows), right side more than left side.

DISCUSSION

As COVID-19 is recognised to cause significant morbidity and mortality, it is imperative to understand its effects on patients with a systemic autoimmune rheumatic disease (SARD) and identify the possible outcomes. Patients with SARD themselves, are known to have an increased risk of mortality 2 – 5 times higher than the general population. This is due to the ongoing defective immune tolerance mechanism and the usage of corticosteroids for the management of most SARD. Patients with SLE have dysregulated type 1 interferon responses and abnormal functionalities of the immune system (1). The use of steroids results in defective phagocytosis and chemotaxis of T cell responses which could further increase the risk of infection in SLE patients. Respiratory infections are one of the most common causes of morbidity and mortality in the elderly with underlying SLE.

Getting COVID-19 infection is associated with poorer outcomes among patients with SLE. A study done in the United States reported that 59% of SLE patients that were tested positive for COVID-19 was hospitalised, with 9% required admission to the intensive care unit, and 9% passed away. The hospitalised patients were much older, from Hispanic ethnicity, either overweight or obese, and had history of lupus nephritis (2).

Our patient developed features of accelerated renal disease such as anaemia, uncontrolled hypertension, and worsening kidney functions relatively two months prior to admission. She had underlying diabetes mellitus type 2 and hypertension, but there was no indication to investigate for other possible causes of renal impairment before. During current hospitalisation, she was diagnosed to have SLE based on positive antinuclear antibody (ANA) and anti-dsDNA with suspicion of lupus nephritis. A study done on the prevalence of autoantibodies post-exposure to SARS-CoV-2 infection showed that up to 30% of COVID-19 patients were detected to have antibodies directed against nuclear or phospholipid antigens (3). While ANA can be detected in severe COVID-19 cases, anti-dsDNA is considered as the hallmark and specific marker for SLE. Presence of anti-dsDNA is virtually diagnostic for SLE, and it has been associated with renal involvement due to its deposition in the kidney structures especially during active nephritis (4). However, renal biopsy was unable to be performed in this patient to confirm the diagnosis of lupus nephritis.

Kidney diseases have also been reported among COVID-19 patients, in the form of acute kidney injury, haematuria, and proteinuria, which are associated with higher mortality rates. The pathogenesis behind kidney injury remains unknown, but it has been postulated that this could be due to direct toxicity from the virus itself or due to haemodynamic changes (5). Steroid usage in COVID-19 was not recommended due to inhibition of viral clearance and prolongation of viraemia phase. A study published earlier showed that mortality rate is increased in those severe COVID-19 patients who received high dose corticosteroids compared to their counterparts who did not receive it. This could explain why this patient deteriorated faster.

In our case, it was challenging to determine whether the rapid decline in kidney function was due to active SLE, COVID-19, or a combination of both diseases that had caused the patient to succumb despite the intensive and aggressive treatments. There is possibility that the

patient could already have had pre-clinical onset or undiagnosed SLE prior to current clinical presentation. However, she had never been investigated for an underlying connective tissue disease before as there was no clinical indication for it. Unfortunately, the unprecedented COVID-19 pandemic also had resulted in congestion at the healthcare facilities and increased appointment interval, leading to delayed diagnosis and compromised patient care.

CONCLUSION

Considering this is a single-case observation, it has many limitations. However, it is of note that concomitant COVID-19 infection could worsen the outcome of SLE, particularly in patients with renal involvement and positive anti-dsDNA.

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