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Editorial

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CHALLENGES OF MANAGING A CASE OF WORSENING ACUTE KIDNEY INJURY IN ACTIVE LUPUS NEPHRITIS WITH SUPERIMPOSED COVID-19 INFECTION: A CASE REPORT

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ABSTRACT

We present a challenging case of a young man with known lupus nephritis who came to us with a flare of lupus nephritis and superimposed COVID-19 infection. The use of immunosuppressant in lupus nephritis flare with concurrent infection remains a concern of igniting overwhelming infection. Despite high dose prednisolone and dialysis, we noticed worsening in his renal function. He subsequently received intravenous immunoglobulin (IVIG) as rescue therapy that resulted in clinically and biochemically improvement. He was discharged to home well with improved renal function. However, future clinical trials are required to conclude our observation if IVIG rescue therapy in an acute flare of lupus nephritis with concurrent COVID-19 pneumonia remains to be a feasible treatment option. Furthermore, the association and causation of acute flare of lupus nephritis caused by COVID-19 infection remain to be explored.

Keywords: *Lupus nephritis, intravenous immunoglobulin, Covid-19*

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disease in which the immune system attacks its tissues, causing widespread inflammation and tissue damage in the affected organs. It can affect the joints, skin, brain, lungs, kidneys, and blood vessels. The prevalence of SLE patients developing Lupus Nephritis (LN) varies between different regions of the world, races, and ethnicities. In the United States, we can see a higher prevalence of LN among black populations. Asian SLE patients have a higher prevalence of LN compared to Caucasian SLE patients. Asians often present with more severe diseases. Up to 10% of LN patients will develop end-stage renal disease (ESRD). The risk of ESRD is higher in a certain subgroup of LN such as Class IV (diffuse LN) which is as high as 44% over 15 years. More importantly, by achieving complete disease remission, the patient 10-year survival rate is 95% as compared to 43% for those with no remission.

The reports for the incidence of COVID-19 patients with an autoimmune disorder were scarce. Despite few case reports having been published on the possible association between autoimmune disorders and COVID-19, the role of this virus in these conditions remains unclear.

CASE PRESENTATION

We report a case of a 28-year-old male with an acute flare of lupus nephritis with concurrent COVID-19 infection. He has a medical history of SLE, and Lupus Nephritis complicated with chronic kidney disease (class IV LN based on renal biopsy on August 2020). He had multiple histories of the flare of lupus nephritis previously, precipitated by non-compliance to medication. His recent flare episode was a week before his admission

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for COVID-19 infection. During the admission for the acute flare on lupus nephritis, he was pulsed with IV Methylprednisolone 500mg daily for 3 days and given a STAT dose of IV Cyclophosphamide 500mg as a part of the EUROLUPUS regime. He was discharged with a tapering dose of prednisolone, hydroxychloroquine and he complied with the treatment this time. At the time of discharge, he was well clinically, and his renal profile improved.

A week after being discharged, he presented with acute onset of fever (38ºC), non-productive cough, progressive dyspnea, and worsening abdominal swelling. He denied any contact with COVID-19 patients and no exposure to high–risk patients during his recent admission.

On physical examination, he was in mild respiratory distress with a respiratory rate of 22 but was able to speak in full sentences. Lung's auscultation revealed reduced breath sound bilateral lower zone and abdominal ascites. Mild pedal edema was also noted to the level of mid-shin. Oxygen saturation was 97% on room air and other vital signs were stable. At his presentation to the emergency department, he did not require any oxygenation support despite mild respiratory distress as saturation was able to maintain > 95% on room air. His initial diagnosis was COVID-19 pneumonia category 3 with lupus nephritis flare.

The first test performed was a COVID-19 Antigen Rapid Test Kit which was positive. His COVID-19 Real-Time – Polymerase Chain Reaction swab had shown a cycle threshold (CT) value of 28. His blood and urine laboratory parameters concurred with the flare of lupus nephritis and acute renal failure (Fig. 1) and his chest X-ray on admission showed bilateral peripheral opacities which is one of the features of COVID-19 Pneumonia. Other laboratory findings showed urea 50.7mmol/L, creatinine 865 µmol/L, eGFR 7 mL/min/1.73m2, CRP 33.65mg/L (normal range < 5mg/L) and WCC 11.2 x109 (normal range 4-11 x109). His baseline renal profile was urea 37mmol/L, creatinine 195umol/L, eGFR 41 one week before admission.

The initial treatment given in the emergency setting was intravenous frusemide 40mg STAT dose with subcutaneous low molecular weight heparin (LMWH) 40mg as DVT prophylaxis. In terms of steroids, he was continued on prednisolone 50mg once daily started on this admission for the acute flare of nephritis. He had urgent hemodialysis via the femoral catheter after consulting a nephrologist.

Throughout his stay inward, we noticed worsening renal function despite adequate urine output and regular dialysis. In terms of COVID-19 pneumonia, there was no disease progression or respiratory distress requiring oxygen support, and it remained at category 3. A decision was made for intravenous immunoglobulin (IVIG) as the lupus flare was not improving despite being given a high dose of prednisolone. IVIG was given a total of 90g in 2 divided doses on day 6 of admission. There was a delay in the initiation of IVIG due to the patient's financial constraints. Renal profile following IVIG had shown improvement with urea 31mmol/L and creatinine 303umol/L. Repeated urine protein: creatinine ratio was 655mg/mmoL (normal range <50mg/mmoL) and urine for examination and microscopy showed protein 3+. The patient improved clinically and biochemically after a few days of IVIG administration. The patient was counseled for a repeat renal biopsy but refused. He was then discharged with a tapering dose of prednisolone and regular frusemide as clinically all the presented symptoms resolved, and his vitals were stable. A nephrology clinic appointment was given 4 weeks after discharged and he was given cyclophosphamide as the continuation of the subsequent EUROLUPUS regime. Renal profile during clinic appointment further improved with urea 20.3mmol/L and creatinine 250umol/L. We summarized the serial laboratory workup in the table below (Table 1.)

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LABORATORY INVESTIGATIONS	Equation Baseline (4 months prior admission)	Baseline (1-week prior admission after given methylprednisolone and cyclophosphamide)	On admission (Before treatment with IVIG)	Upon discharge (After treated with IVIG)	During renal clinic appointment (After discharge)
Hb (13-17g/L)	14.7	14.9	13.0		
WCC (4-10 x10^9)	3.7	5.2	11.2		
PLT (150-400 ¯x10^9)	158	172	206		
CRP (<5.00mg/L)		4.85	33.65	3.44	6.35
ESR (<21mm/hr)		23	45		11
Urea (3.2-8.2mmol/L)	6.5	37	50.7	31	20.3
Creatinine (54-97umol/L)	87	195	865	303	250
Urine PCR UFEME	341.6 3+	689 3+	1029 3+	655 3+	545.1 3+
Anti-dsDNA (0-200iU/mL)			148		52
C3 (90-180mg/dL)			80		112
C4 (10-40mg/dL)			44		49

Table 1. Laboratory investigations at baseline, during admission, upon discharge, and during renal clinic appointments.

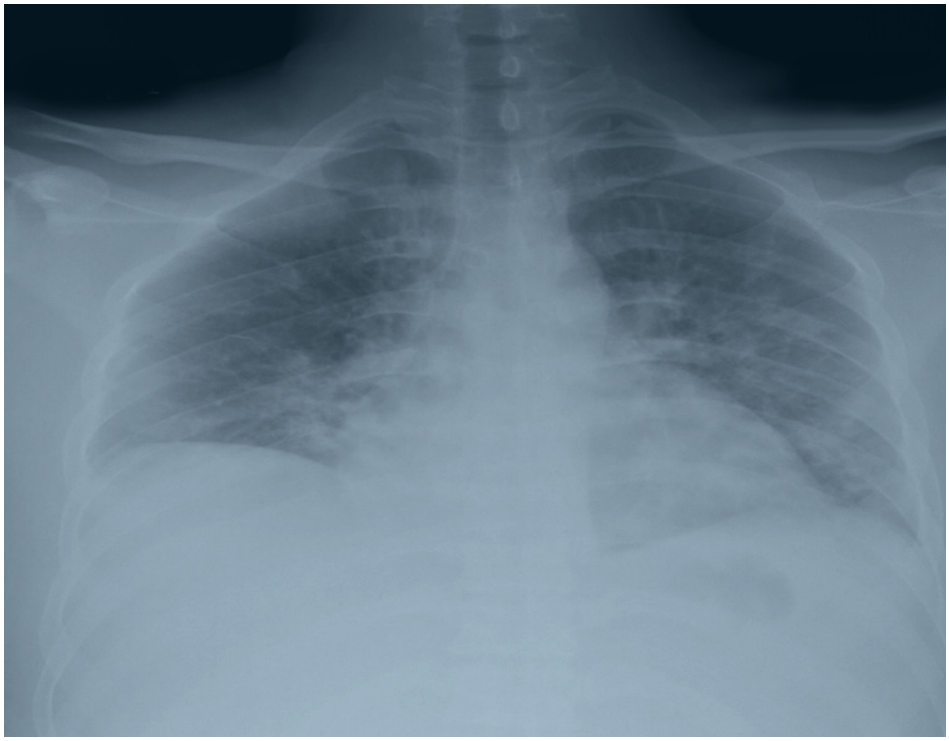

Fig. 1. Chest X-Ray depicting bilateral interstitial infiltrates which are the features of both lupus nephritis and COVID-19 Pneumonia

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DISCUSSION

In this case report, a puzzling scenario was encountered. Our patient had COVID-19 Pneumonia with a concurrent acute flare of lupus nephritis. His presenting symptoms of fever, cough, shortness of breath, abdominal distension, and bilateral lower limb swelling can be observed both in lupus and COVID-19 Pneumonia. Lymphopenia on the other hand can be a hallmark feature in both disorders. Previous studies reported that certain viruses may be related to the pathophysiology of SLE flare. Epstein-Bar virus (EBV), cytomegalovirus, and parvovirus B19 are some of the many possible triggers for SLE. There is also a reported case of dengue fever evolving into a lupus flare. They found that the dengue virus has triggered a dysfunctional immune response that resulted in the development of SLE, lupus nephritis [1]. Otherwise, the exact pathophysiology behind it remains unclear.

There are limited data on the association and causation of COVID-19 pneumonia triggering lupus nephritis flare; and the treatment option for lupus nephritis flare during COVID-19 pneumonia. One case reported from Kashan Rheumatology Clinic showed that the patient developed a flare of lupus nephritis after 2 months post COVID-19 infection. The patient was treated with methylprednisolone for 3 days, maintenance of prednisolone and hydroxychloroquine, and his symptoms improved [3]. Another case was reported in Riyadh, Saudi Arabia, where COVID-19 infection triggered a lupus flare, lupus pneumonitis. The patient was treated with methylprednisolone and tapering oral steroids and was discharged well [4]. Our approach was different from the above-reported cases whereby we used IVIG as rescue therapy in the case of acute flare during the acute phase of COVID-19 infection.

Our patient was initially treated with high-dose prednisolone to cover both COVID-19 and flare of lupus nephritis. However, due to the worsening renal function despite on high dose prednisolone and dialysis, he was decided for intravenous Immunoglobulin (IVIG). This IVIG rescue therapy was deemed to be the best option to treat acute flare of resistant lupus nephritis moreover with the presence of ongoing infection, in this case, COVID-19 pneumonia. IVIG has been proven to be effective in treatment-resistant membranous or membranoproliferative lupus nephritis [2]. Besides, observations have been reported that IVIG can potentially be an effective adjunct treatment for COVID-19 pneumonia. A pilot study in San Diego, California reported that IVIG 0.5 g/kg daily for 3 days with concomitant methylprednisolone 40 mg reduced progression of respiratory failure requiring mechanical ventilation, the total length of hospital stay, and ICU length of stay, and improved oxygenation at 7 days in COVID-19 patients [5]. Shao et al identified that early IVIG administration significantly reduces the 28-day mortality rate, improves some organ functions, and decreases inflammatory response in severe COVID-19 patients [6]. This can be explained by the fact that viremia develops within the first week of infection. Subsequently, the primary immune response emerges in the blood circulation by day 10–14 and is followed by viral clearance. Additionally, FJF Herth et al demonstrated that IVIG appeared to improve the clinical symptoms, chest imaging, and laboratory investigations. Patients who received IVIG earlier showed a shorter duration of hospital stay [7]. These reports possibly explain why our patient did not progress to the worsening category of COVID-19 pneumonia.

Nevertheless, P Tabarsi et al did not support the use of IVIG in combination with hydroxychloroquine and lopinavir/ritonavir in the treatment of severe COVID-19 cases [8]. The usage of IVIG in the case of acute lupus flare with concurrent COVID-19 infection remains uncertain especially in the Asian population who has more aggressive lupus nephritis. To date, COVID-19 Treatment Guidelines Panel recommends against the use of IVIG for the treatment of acute COVID-19, except in clinical trials.

CONCLUSION

Our case report illustrated that IVIG rescue therapy for an acute flare of lupus nephritis in the presence of ongoing COVID-19 pneumonia can be potentially a feasible and safe treatment. However, future clinical trials are required to conclude our observation as the current treatment for COVID-19 pneumonia perse do not recommend the use of IVIG. Furthermore, the association and causation of acute flare of lupus nephritis caused by COVID-19 infection remain to be explored.

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